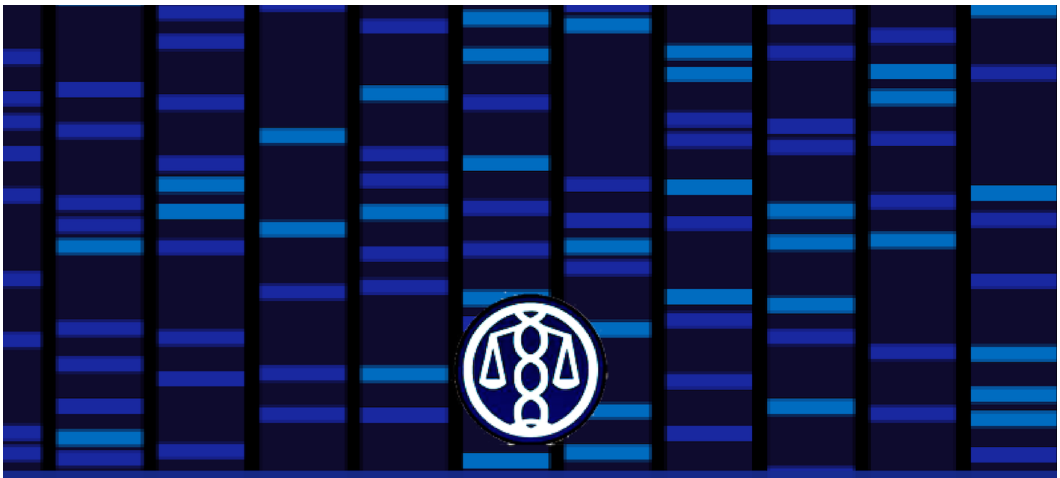
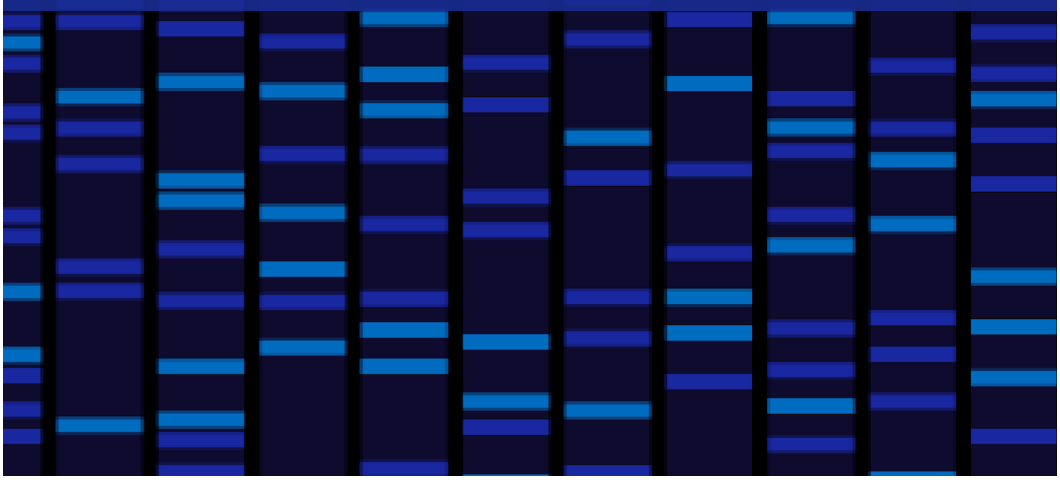


Centre for Law and Genetics
Occasional Paper No 9

D'ARCY V MYRIAD GENETICS

The Impact of the High Court's Decision on the Cost of Genetic Testing in Australia

DIANNE NICOL, JANE NIELSEN AND VERITY DAWKINS



D'ARCY V MYRIAD GENETICS: THE IMPACT OF THE HIGH COURT'S DECISION ON THE COST OF GENETIC TESTING IN AUSTRALIA

Dianne Nicol, Jane Nielsen and Verity Dawkins

Centre for Law and Genetics

University of Tasmania

Occasional Paper No 9

National Library of Australia Cataloguing- in- Publication Data

ISSN 1445-2766

This issue may be cited as

Dianne Nicol, Jane Nielsen and Verity Dawkins, '*D'Arcy v Myriad Genetics:* The Impact of the High Court's Decision on the Cost of Genetic Testing in Australia' (Occasional Paper No 9, Centre for Law and Genetics, 2018).

Published by

Centre for Law and Genetics

Faculty of Law

University of Tasmania

Private Bag 89

Hobart Tasmania 7001

Australia

Printed by

Mercury Walch

5 Bowen Road

Moonah Tasmania 7009

Australia

PREFACE

This occasional paper is the result of a study funded by IP Australia looking into the effects of the High Court's decision in *D'Arcy v Myriad Genetics* [2015] HCA 35 on the cost of genetic diagnostic testing in Australia. The High Court handed down its decision on 7 October 2015, and this study sought to ascertain whether there is any basis to conclude that the decision, which invalidated Myriad's patent over the BRCA gene, has had a discernible impact on the cost of testing. In addition to reviewing the extensive literature that has amassed in relation to patents and their impact on genetic diagnostic testing, the project involved detailed analysis of relevant case law and interviews with those involved in genetic testing in Australia.

We extend our sincere thanks to IP Australia for enabling this important research. This study was funded by IP Australia but the results reported in no way reflect the views of IP Australia or the Australian Government. We are indebted to all of our participants for so generously giving their time to be interviewed. We also thank Bryanna Workman for her invaluable work in editing and putting this occasional paper together.

A summarised version of this occasional paper has been accepted for publication in the *European Intellectual Property Review*:

> Jane Nielsen and Dianne Nicol, 'The Myriad Litigation and Genetic Diagnostic Testing in Australia' (2019) *European Intellectual Property Review* (forthcoming).

We have permission from the editors of the *European Intellectual Property Review* to publish material from that article in this occasional paper.

The authors have no conflicting interests. To the best of our knowledge the law as stated in this occasional paper is current as at 31 December 2018.

TABLE OF CONTENTS

CHAPTER 1

INTRODUCTION

This occasional paper provides an assessment of whether the decision of the High Court of Australia in *D'Arcy v Myriad Genetics Inc* ('*D'Arcy*')[1] has had any significant impact on the cost of diagnostic testing in this country. Our hypothesis in undertaking the study was that the decision would have had very little impact on the pricing of genetic diagnostic testing in Australia, based on our past research in this area and our knowledge of the legal and business landscape. In testing this hypothesis, we first briefly outline the nature of the patent claims in issue in *D'Arcy* and other relevant cases, the law relating to the patentable subject matter inquiry, and the details of the *D'Arcy* decision and its sequelae.

We then provide a brief overview of the genetic diagnostic testing industry and summarise earlier research findings on patent subsistence, enforcement and costs to providers of genetic diagnostic testing services. Next, we turn to the empirical aspect of our study, which has been designed to provide evidence of the extent to which the *D'Arcy* decision has had, or is likely to have an impact on the current costs of genetic diagnostic testing services. This evidence takes the form of data collected from interviews with individuals from facilities involved in the provision of genetic diagnostic testing services, and individuals responsible for setting fees and reimbursement schedules for the provision of genetic diagnostic testing services in state and federal health departments and the private sector. In the last section of the occasional paper, we consider other implications of patents claiming rights to nucleotide sequences and to other subject matter (particularly method claims), both for the genetic diagnostic testing sector and for other industry sectors.

To be clear, we have focused solely on the issue of cost in this study – primarily whether invalidation of the patents held by Myriad Genetics, Inc ('Myriad') could have the effect of decreasing the cost burden on providers of genetic diagnostic testing by invalidating patents that ostensibly have been responsible for creating that same cost burden. We have not undertaken an analysis of the purported benefits arising from the grant of Australian patents to Myriad (nor other nucleotide sequence and method patents). This is beyond the scope of this study. The question

[1] *D'Arcy v Myriad Genetics Inc* (2015) 258 CLR 334; [2015] HCA 35 (7 October 2015) ('*D'Arcy*').

of whether patents of this nature contribute to the incentive function of the patent system is a vexed one, which has not been resolved empirically in any jurisdiction.

In the context of the *D'Arcy* case, we note that, over a number of years, Myriad filed various patents over the BRCA1 and BRCA2 nucleotide sequences and their methods of use in multiple jurisdictions.[2] Discovery of the link between BRCA1 and BRCA2 mutations and increased risk of developing breast and ovarian cancer was an important development. It led to the development of genetic diagnostic tests that are used to identify whether individual patients possess mutations in their BRCA nucleotide sequences that are known to be associated with a much higher than average risk of developing breast or ovarian cancer. Diagnostic tests can also be used to detect BRCA mutations in breast cancer tumour cells, facilitating decision-making about treatment options that are only available to patients who test positive to the relevant mutations.

Myriad acquired particular benefit from the exercise of its patent rights in the US (though, as we will see, less so in Australia) by insisting on exclusivity in provision of BRCA testing. As a result, Myriad now possesses a database of sequence information that is far superior to public databases, or databases of any of its competitors, in that there is a much lower percentage of sequence variants of unknown significance. This means that Myriad can give a much more accurate report on the presence or absence of deleterious mutations linked with increased susceptibility to the development of breast and ovarian cancers. Quite whether this is of benefit to society is another question entirely. Those individuals receiving BRCA test results from Myriad may have a more accurate diagnosis than if they go to another provider. The problem is that there is no indication that Myriad is prepared to give open access to this database, providing it with a competitive advantage going beyond the term of its (now invalidated) US patents, and potentially leading to significant disadvantage to those patients who cannot access Myriad tests.[3] Although some anecdotal comments suggest that the quality of

[2] We note that the terms nucleotide sequences, DNA, genes and nucleic acids are used interchangeably in the primary and secondary literature. We have adopted the terminology of nucleotide sequences in this report, except when quoting or referring to sources that use different terminology.

[3] We discuss this further in Jane Nielsen and Dianne Nicol, 'The Legal Vacuum Surrounding Access to Gene-Based Materials and Data' (2016) 24 *Journal of Law and Medicine* 72.

data held in public databases will soon be on par with Myriad's, a recent analysis suggests that they are still a long way apart.[4]

[4] William Gradishar et al, 'Clinical Variant Classification: A Comparison of Public Databases and a Commercial Testing Laboratory' (2017) 22(7) *Oncologist* 797 doi: 10.1634/theoncologist.2016-0431.

CHAPTER 2

METHODS

This study utilised mixed methods in an effort to drill down on whether *D'Arcy* has had a measurable impact on the cost of genetic diagnostic testing in Australia. Methods included:

- detailed searches of relevant legal, IP and other databases and websites for information on the *D'Arcy* decision and the makeup of the Australian genetic diagnostic testing industry;
- doctrinal analysis of the *D'Arcy* decision and other case law;
- detailed review of empirical literature considering the impact of nucleotide sequence patents on the delivery of genetic diagnostic testing; and
- interviews with key stakeholders in the Australian genetic diagnostic sector.

The interview component of this study involved interviews with key personnel from the genetic diagnostic testing industry in Australia. Ethics approval for this interview component was granted by the Tasmania Statewide Human Research Ethics Committee.[5] Participants were selected using purposive and critical case sampling techniques. Labs that perform genetic diagnostic tests were identified through the databases of the Royal College of Pathologists of Australia and the National Association of Testing Authorities. These databases are publicly available and contained on the websites of these organisations. The contacts obtained were cross-checked to assist in identifying relevant personnel within each organisation. The total number of labs listed was 45: this included both public and privately-run labs, and was based on the listing contained in Table 3 of this occasional paper.

A significant number of the labs listed were contacted: in all, 40 emails were sent to relevant personnel. In some cases, more than one person within an organisation was contacted where it became apparent that an alternative contact would be more likely to yield an interview. We were particularly interested in speaking with participants from public labs

[5] Tasmania Statewide Human Research Ethics Committee Minimal Risk Application H0016230, 30 November 2016.

offering a large number of available tests. Labs offering BRCA testing were also targeted given our specific interest in the effect of the *D'Arcy* decision. State health department contacts were identified by internet searches. All of the private providers were contacted. We continued to seek interviews until thematic saturation was reached. Interviews were based on a number of interview themes developed around the core research question (see Appendix A). Using our analysis of literature, case law and previous empirical studies, we were able to derive a conceptual framework against which to conduct iterative data analysis. De-identified transcripts were coded and analysed. Thematic and latent content analysis techniques were employed to inductively analyse our data,[6] with findings from interviews being progressively fed into subsequent interviews.

Sixteen interviews were conducted. Table 1 contains a categorisation of interviewees and demonstrates a fairly even spread across industry sectors.

Table 1: Categories of interviewees

	State health department	Pathology labs in public hospitals	Standalone public pathology labs and other non-profit providers	Research institutes/ universities	Private companies
Number interviewed	3	4	3	3	3
Number involved in provision of BRCA testing	2	1	3	2	1

[6] Maria J Mayan, *Essentials of Qualitative Inquiry* (Left Coast Press, 2009).

CHAPTER 3

THE D'ARCY DECISION AND ITS BROADER IMPACT

3.1 PATENT CLAIMS IN ISSUE

As intimated in the introduction to this occasional paper, our analysis focuses primarily on two types of patent claims, nucleotide sequence claims and method claims. Critically, the courts in *D'Arcy* considered only nucleotide sequence claims because these were the only claims that were challenged by the applicant. We do not know the exact reason why the applicants chose only these claims. However, we have seen in our earlier work and in our current round of interviews that there is a deep-seated view among Australian test providers that patents should not be available for isolated nucleotide sequences. This concern does not appear to extend to claims relating to methods of diagnosis, even though they, like sequence claims, can be used to provide exclusivity in the genetic diagnostic testing market. In contrast, in US litigation corresponding with the Australian *D'Arcy* case, the applicants challenged both sequence and method claims. However, like the *D'Arcy* decision, the final decision by the US Supreme Court in this case, *Association for Molecular Pathology v Myriad Genetics Inc* ('*AMP'*)[7] concerned only nucleotide sequence claims. Moreover, neither court specifically ruled on modified/human made sequences (other than cDNA sequences, which are explained below); sequences incorporated into pharmaceutical products; other products of nature; or methods.

3.1.1 Nucleotide sequence claims

Within the set of nucleotide sequence claims that were included in Myriad's patents, a distinction can be drawn between isolated nucleotide sequences (sometimes referred to as gDNA) and complementary DNA (cDNA). An isolated sequence is a sequence of nucleotides derived from a DNA molecule that has been removed from its normal cellular environment, without modification.[8] In *D'Arcy*, some of the isolated

[7] *Association for Molecular Pathology v Myriad Genetics Inc,* 133 US 2107 (2013) ('*AMP*').

[8] *D'Arcy* (2015) 258 CLR 334, 360.

nucleotide sequence claims were to the entire genes, whereas others claimed much shorter sequences occurring within the genes.[9]

In contrast to an isolated nucleotide sequence, cDNA is not precisely the same as a nucleotide sequence existing in nature, since it is reverse transcribed from messenger RNA.[10] Messenger RNA (mRNA) is an intermediary in the process of formation of protein based on the information contained in genes. In the process of transcription from genes to mRNA, parts of the nucleotide sequence included in the genes (the introns) are removed. As such, cDNA only includes the active parts of the nucleotide sequence in genes used in protein formation (exons). Despite these informational differences, the functions of the isolated nucleotide sequences and cDNA derived from a particular gene are essentially the same, in that both are capable of coding for the same protein.[11]

The principal nucleotide sequence claim in *D'Arcy* that was in dispute was claim 1:

> *[a]n isolated nucleic acid coding for a mutant or polymorphic BRCA1 polypeptide, said nucleic acid containing in comparison to the BRCA1 polypeptide encoding sequence set forth in SEQ.ID No:1 one or more mutations or polymorphisms selected from the mutations set forth in Tables 12, 12A and 14 and the polymorphisms set forth in Tables 18 and 19.*

The patent specification explains that a combination of sequences obtained from cDNA clones, hybrid selection sequences and amplified PCR[12] products allowed construction of a composite full length sequence for BRCA1 cDNA designated SEQ ID No:1.[13] Even though the claimed sequence was artificially constructed, the High Court held that it was invalid because it contained no new information. Rather, it was 'the same

---

9 Dianne Nicol, '*Myriad Genetics* and the Remaining Uncertainty for Biotechnology Inventions' in Charles Lawson and Berris Charnley (eds), *Intellectual Property and Genetically Modified Organisms: A Convergence in Laws* (Ashgate, 2015) 123, 129–130.

10 Ibid.

11 Ibid.

12 PCR is the polymerase chain reaction, a foundational technique that enabled amplification of DNA strands for use in experimentation: Randall K Saiki et al, 'Enzymatic Amplification of Beta-globin Genomic Sequences and Restriction Site Analysis for Diagnosis of Sickle Cell Anemia' (1985) 230 *Science* 1350; Kary Mullis, 'The Unusual Origin of the Polymerase Chain Reaction' (April 1990) *Scientific American* 56.

13 *D'Arcy* (2015) 258 CLR 334, 364.

information as that contained in the DNA of the person from which [it] was isolated'.[14]

In *AMP* nine nucleotide sequence claims from three patents were in issue.[15] The Court stated that claims 1, 2, 5, and 6 from a patent they identified as the '282 patent were representative. Of these, claims 1 and 5 referred to gDNA whereas 2 and 6 were cDNA claims. Claim 1 was similar, but not identical to its equivalent in Australia: an isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.[16] Claim 2 was in similar terms, but only referenced the cDNA sequence. Claims 5 and 6 claimed only a subset of the nucleotides in the BRCA gene: an isolated DNA having at least 15 nucleotides of the DNA of claim 1 (or 2). The Supreme Court found that claims 1 and 5 were invalid, but not claims 2 and 6. These claims were held to be valid by the Supreme Court because 'creation of a cDNA sequence from mRNA results in an exons-only molecule that is not naturally occurring.'[17] The Court found that something unquestionably new is created when cDNA is made. Therefore, cDNA did not fall within the 'product of nature' exception, and was patent eligible.

3.1.2 Method claims

As stated above, method claims were not in issue in *D'Arcy.* In contrast, two types of method claims were in issue in *AMP*: broad methods of diagnosis, underlaid by sequence information; and specific methods of diagnosis, also underlaid by sequence information. The validity of these claims was determined on two occasions by the Court of Appeals of the Federal Circuit.[18] The decisions of the Federal Circuit in relation to the method claims were not appealed by either party in the Supreme Court.

The broad claims were to methods of analysing or comparing a patient's BRCA sequence with the normal, or wild type, sequence to identify the

---

14 Ibid 371.

15 *AMP,* 133 US 2107, 2113 (2013).

16 Ibid 2113.

17 Ibid 2119.

18 *Association for Molecular Pathology v United States Patent and Trademark Office*, 653 F 3d 1329, 1334 (Fed Cir, 2011); *Association for Molecular Pathology v United States Patent and Trademark Office*, 689 F 3d 1303, 1335 (Fed Cir, 2012). The Federal Circuit was required to hear the case a second time because the US Supreme Court would not grant certiorari before the lower court had the opportunity to consider whether the intervening Supreme Court decision in *Mayo Collaborative Services v Prometheus Laboratories Inc,* 566 US 66 (2012) had any bearing on its decision in *AMP*. In essence, the original decision of the Federal Circuit remained unchanged in the second decision.

presence of cancer predisposing mutations, whether in the form of germline mutations in the patient's cells, or specific somatic mutations in tumour cells.[19] The courts considered claim 1 of the patents they referred to as the '999 and '001 patents to be representative of all but one of the method claims.

Claim 1 of the '999 patent provided:

> *[a] method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables 12A, 14, 18 or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO: 1.*[20]

Claim 1 of the '001 patent provided:

> *[a] method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises … comparing a first sequence selected from the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample.*[21]

These claims were found to be too broad in both the first and second decisions of the Federal Circuit. In the first decision Justice Lourie stated that they were not patentable because they claimed only abstract mental processes, and that the comparison between the two sequences can be

---

19 *Association for Molecular Pathology v United States Patent and Trademark Office*, 653 F 3d 1329, 1334 (Fed Cir, 2011).

20 Ibid.

21 Ibid 1335.

accomplished by mere inspection alone, not through any determination or transformative step.[22] This was affirmed in the second decision.[23]

More specificity and the inclusion of transformative steps can make a method patent valid. In the Federal Circuit Court decision, claim 20 of the patent referred to as '282 was distinguished from the other method claims. It provided:

> *[a] method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic, growing said transformed eukaryotic host cell in the absence of said compound, determining the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cell in the absence of said compound and comparing the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic.*[24]

This claim was held patent eligible in both decisions of the Federal Circuit.[25] It was found valid because 'in addition to the step of comparing the cells' growth rates, the claim also recites the steps of growing transformed cells and determining those growth rates.'[26] These steps were held to be transformative.[27] It was concluded that the product of claim 20 was a transformed cell, man-made and not naturally occurring.[28]

Table 2 provides a summary of the four types of claims in issue in the US litigation, and the holdings of the courts at each decision level. [29]

---

22 Ibid 1355.

23 *Association for Molecular Pathology v United States Patent and Trademark Office*, 689 F 3d 1303, 1335 (Fed Cir, 2012).

24 *Association for Molecular Pathology v United States Patent and Trademark Office*, 653 F 3d 1329, 1335 (Fed Cir, 2011).

25 First Federal Circuit decision: *Association for Molecular Pathology v United States Patent and Trademark Office*, 653 F 3d 1329, 1358 (Fed Cir, 2011); Second decision: *Association for Molecular Pathology v United States Patent and Trademark Office*, 689 F 3d 1303, 1337 (Fed Cir, 2012).

26 *Association for Molecular Pathology v United States Patent and Trademark Office*, 689 F 3d 1303, 1335 (Fed Cir, 2012).

27 Ibid 1333–4.

28 Ibid.

29 Extracted from: Nicol, above n 9, 130–1.

Table 2: Summary of decisions in the AMP case

	Isolated sequences identical to those in nature (gDNA)	Synthetic sequences complementary to RNA (cDNA)	Methods of comparing or analysing DNA sequences	Method for screening potential cancer therapeutics
***AMP* First Instance** **Sweet J**	Invalid – products of nature. Physical embodiment of information – structural and functional differences irrelevant	Not distinguished from gDNA	Invalid – abstract mental processes No machine or transformation[1]	Invalid – basic scientific principle No machine or transformation
***AMP* Federal Circuit, #1 and #2** **Lourie J (majority)**	Valid – markedly different chemical identity and nature – broken covalent bonds	Valid – markedly different	Invalid – abstract mental processes. No additional transformative steps included in the claims	Valid – transformative. Growing and determining growth rates of transformed cells
***AMP* Federal Circuit #1 and #2** **Moore J (majority)**	Valid – chemical differences are not enough and no new utility – not a blank canvas – leave intact settled expectations	Valid – joined majority	Invalid – joined majority	Valid – joined majority
***AMP* Federal Circuit #1 and #2** **Bryson J (dissent in part)**	Invalid – products of nature – same structurally and functionally – the only changes were incidental to extraction	Generally valid – agreed with the majority except for claims to short strands indistinguishable from gDNA.	Invalid – joined majority	Valid – joined majority
***AMP* SCOTUS**	Invalid – products of nature. Isolation from surrounding genetic material is not enough	Generally valid – markedly different, except for the claims identified by Bryson J	Not decided	Not decided

3.2 PATENTABILITY OF NUCLEOTIDE SEQUENCES PRE-*D'ARCY*

Prior to the *D'Arcy* decision, nucleotide sequences were generally considered patentable if they satisfied legislative requirements included in the *Patents Act 1990* (Cth) ('*Patents Act'*), (as were claims to methods of diagnosis). A patentable invention, as defined in the *Patents Act,* requires *inter alia* the subject matter of a claim to be a 'manner of new manufacture' within the meaning of section 6 of the *Statute of Monopolies 1623.* Prior to *D'Arcy,* the seminal authority on the meaning of manner of manufacture was *National Research Development Corporation v Commissioner of Patents* in 1959 ('*NRDC*').[30] The two key elements required for satisfaction of the manner of manufacture requirement articulated by the High Court in this case were: 'is it an artificially created state of affairs of economic utility?'[31] As the biotechnology industry emerged in the 1980s and 1990s it was widely thought that genetic materials made in the lab satisfied this requirement because they were isolated from the natural environment and had economic value to the Australian industry and to healthcare generally.[32]

Kirin-Amgen Inc v Board of Regents of University of Washington in 1995 was the first reported decision of the Australian Patent Office which considered whether to allow a patent claim to isolated nucleotide sequences.[33] The Deputy Commissioner of Patents found that purified and isolated nucleotide sequences were an artificially created state of affairs.[34] Subsequent to this case, granting patents on isolated nucleotide sequences became an established practice.[35] Prior to *D'Arcy,* the Australian courts were not provided with the opportunity to determine whether or not subject matter of this nature satisfied the manner of manufacture requirement.

---

30 *National Research Development Corporation v Commissioner of Patents* (1959) 102 CLR 252 ('*NRDC*').

31 Ibid 276.

32 Dianne Nicol, 'Should Human Genes be Patentable Inventions under Australian Patent Law?' (1996) 3 *Journal of Law and Medicine* 231, 237.

33 *Kirin-Amgen Inc v Board of Regents of University of Washington* (1995) 33 IPR 557.

34 Ibid 569.

35 Emanuela Gambini, 'In the Aftermath of *D'Arcy v. Myriad Genetics Inc*: Patenting Isolated Nucleic Acids in Australia' (2016) 7(2) *European Journal of Risk Regulation* 451, 457.

3.3 LAW REFORM INQUIRIES

One of the key issues for consideration in *D'Arcy* was whether according patentability to the class of claim at issue would involve law making of a kind which should be done by the legislature. Myriad had submitted that the decisions by the legislature and other government bodies not to specifically exclude nucleotide sequences from patentability meant that they should be patentable. One of the first of such discussions occurred in 1990 where the Senate rejected an amendment to the Patents Bill 1990 (Cth) proposed by Senator Coulter, which would have had the effect of excluding nucleotide sequences and genetically modified organisms from patentability.[36] The rationale provided for rejecting the amendment was that it would hinder research and development of new technology in the medical and pharmaceutical fields.[37]

In 2004, the Australian Law Reform Commission released their Report, *Genes and Ingenuity: Gene Patenting and Human Health*, concluding that 'a new approach to the patentability of genetic materials is not warranted at this stage in the development of the patent system'.[38] The ALRC found that the problem regarding access to healthcare was not in the patenting of genetic material and technologies *per se*, but in the way in which those patents may be commercially exploited, including through aggressive licensing.[39]

In November 2010, the Senate Community Affairs References Committee published their Report, *Gene Patents,* following a referral from the Australian Senate. Concerns had been raised in the Senate about the risk that a small Melbourne biotechnology company, Genetic Technologies Ltd ('GTG'), would enforce patents relating to BRCA1 and BRCA2.[40] GTG held an exclusive licence within Australia and New Zealand to exploit the BRCA1 and BRCA2-related patents owned by Myriad. The Committee discussed the proposal for an express prohibition on nucleotide sequence patents but found that a lack of relevant data meant they were

---

36 Commonwealth, *Parliamentary Debates*, Senate, 17 September 1990, 2478–82 (John Coulter).

37 Commonwealth, *Parliamentary Debates,* House of Representatives, 16 October 1990, 2948 (Geoffrey Prosser).

38 Australian Law Reform Commission, *Genes and Ingenuity: Gene Patenting and Human Health*, Report No 99 (2004) [6.53].

39 Ibid [504].

40 Community Affairs References Committee, Parliament of Australia, *Gene Patents* (2010).

unable to conclude whether patents did have an adverse impact on healthcare. As such, they were reluctant to support the introduction of an express exclusion at that time.

Also in 2010, the Advisory Council on Intellectual Property released their Report, *Patentable Subject Matter*, which aligned closely with the Community Affairs References Committee Report. The Council found no persuasive case to introduce a specific exclusion to prevent the patenting of nucleotide sequences and genetic products and declined to recommend the introduction of such a specific exclusion.[41]

In September 2011, the Legal and Constitutional Affairs Legislation Committee completed their Report considering whether to pass the Patent Amendment (Human Genes and Biological Materials) Bill 2010 (Cth).[42] The Bill was introduced into the Senate on 24 November 2010 by Senators Coonan, Heffernan, Siewert and Xenophon. The purpose of the Bill was to amend the *Patents Act* to exclude human genes and biological materials as they exist in nature, from patent eligibility.[43] After receiving 122 submissions and conducting two public hearings, the Committee recommended that the Senate should not pass the Bill. This was mostly due to ambiguities in the drafting which meant that the Bill would not meet its intention, and could have widespread unintended consequences as well as negatively affect innovation.

Cumulatively, these Reports show a clear lack of support for an express exclusion of nucleotide sequences. In contrast, they did support other reforms to the *Patents Act.* In particular, they led to the introduction of an experimental use exemption in 2012, which clarified that experiments on patented inventions do not constitute patent infringement.[44] Other amendments were made in the same amending Act to the inventive step and utility requirements, but the manner of manufacture requirement remained untouched.

41 Advisory Council on Intellectual Property, Commonwealth of Australia, '*Patentable Subject Matter: Final Report'* (2010) 60.

42 Legal and Constitutional Affairs Legislation Committee, Parliament of Australia, *Patent Amendment (Human Genes and Biological Materials) Bill 2010* (2011).

43 Ibid 1.1.

44 *Intellectual Property Laws Amendment (Raising the Bar) Act 2012* (Cth) s 119C.

3.4 THE *D'ARCY* CASE

3.4.1 Case history

The core Australian BRCA1 patent that was the subject of challenge in the *D'Arcy* case was entitled 'In vivo mutations and polymorphisms in the 17q-linked breast and ovarian cancer susceptibility gene', with patent number 686004 ('the 686004 patent'), which had a priority date of 12 August 1994. The patent application was filed in Australia on 11 August 1995 and expired on 11 August 2015, almost two months before the *D'Arcy* decision was handed down by the High Court.

In May 2003, Myriad granted GTG its exclusive licence for the use of Myriad's patents. In 2003 and again in 2008, GTG threatened to enforce their patent rights against public laboratories and research bodies, seeking to prevent these organisations from engaging in any further testing for the BRCA mutations.[45] This resulted in a public backlash. As a result of this public outcry, GTG stated in a report to shareholders on 9 July 2003 that it was not seeking to enforce its rights over the genes and that the BRCA genes 'are our gift to the Australian people'.[46] After GTG attempted to change its policy to enforce its patent rights in 2008, the company then announced that it had reviewed its decision and 'resolved to immediately revert to its original decision to allow other labs in Australia to freely perform BRCA testing'.[47]

In 2010 Cancer Voices Australia and Yvonne D'Arcy launched action against Myriad in the Federal Court challenging the 686004 patent on the sole ground that the claims to nucleotide sequences were invalid because they failed to satisfy the manner of manufacture requirement. Cancer Voices is a non-profit association, and Yvonne D'Arcy is a breast cancer sufferer. Although Cancer Voices became unincorporated during the course of proceedings, Ms D'Arcy was able to continue her case all the way to the High Court. Figure 1 shows a timeline of the case history. These points are elaborated below.

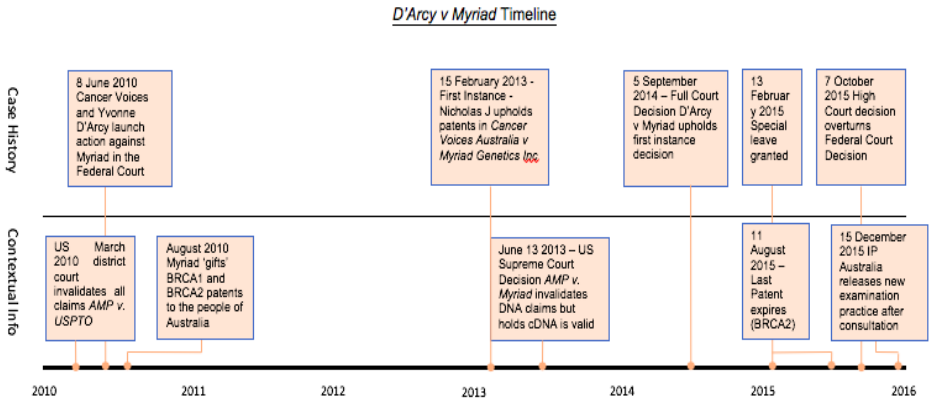
---

45 Dianne Nicol and John Liddicoat, 'Do Patents Impede the Provision of Genetic Tests in Australia?' (2013) 37(3) *Australian Health Review* 281.

46 Genetic Technologies Ltd, 'A Report to Shareholders' (Annual Report, 9 July 2003) 1.

47 Genetic Technologies Ltd, 'New Position re BRCA Testing' (Press Release, 2 December 2008) 1.

Figure 1: The timeline of the D'Arcy litigation



On 15th February 2013, the claims in issue were upheld at the first instance by Justice Nicholas.[48] The key aspect of Nicholas J's decision was that '[i]solated nucleic acid is the product of human intervention involving the extraction and purification of the nucleic acid found in the cell'.[49] In essence, then, for Nicholas J the simple act of isolation of nucleotide sequences from a cell was enough to satisfy the 'artificially created state of affairs' component of the test in *NRDC*.[50] The *NRDC* test requires both that the claimed subject matter (in that case a process of ridding weeds from crop fields) produces an artificially created state of affairs, and that it belongs to the useful rather than fine arts – that it is in the field of economic endeavour.[51] The second limb was not in issue in the *D'Arc*y case.[52]

On 15th September 2014, Chief Justice Allsop and Justices Dowsett, Kenny, Bennett and Middleton of the Full Federal Court upheld Justice Nicholas' first instance decision.[53] However, their reasoning was somewhat more nuanced. For their Honours, there was more to the invention than the simple removal of a nucleotide sequence from the inside of a cell. Their Honours held that 'the claimed product is not the same as the naturally occurring product. There are structural differences but, more importantly, there are functional differences because of isolation'.[54] In concluding, their Honours emphasised that the case is not

48 *Cancer Voices Australia v Myriad Genetics Inc* (2013) 99 IPR 567; [2013] FCA 65.

49 Ibid [104].

50 *NRDC* (1959) 102 CLR 252.

51 Ibid 277.

52 *D'Arcy v Myriad Genetics Inc* (2014) 224 FCR 479, 510 [172].

53 Ibid.

54 Ibid 517 [212].

about the wisdom of the patent system, nor the policy, moral and social reasons for excluding nucleotide sequences from patenting.[55] Rather, it is about the law, and whether the principles articulated in *NRDC* apply. The first of five key features of the subject matter of the claim illustrates the essence of the core patent claim that led to their decision to uphold validity: 'It is to a compound; a nucleic acid. It is not a claim to information'.[56]

On 13th February 2015, special leave was granted to appeal to the High Court.

3.4.2 The High Court decision

As noted earlier in this occasional paper, the High Court unanimously allowed the appeal, holding that the invention claimed did not fall within the concept of a manner of manufacture. Here, some of the key aspects of the reasoning of the judges in *D'Arcy* are explored. There were three separate judgments:

Plurality – French CJ, Kiefel, Bell and Keane JJ

The *D'Arcy* case is notable because of the way in which the plurality in that case refocused attention on the precise nature of the reasoning in *NRDC*. While acknowledging that in many instances the two-limb test will be sufficient, the plurality held that in some circumstances where the claims do not fall within the established boundaries of patentable subject matter it is necessary to look to a range of other factors.[57] In the context of nucleotide sequences, even if the two-limb test were to be applied in isolation, the plurality held that the 'artificially created state of affairs' requirement would not be satisfied because in substance the claims were to information.[58] Ms D'Arcy submitted that none of the chemical, structural or functional differences play any part in the definition of the invention, which is essentially the information.[59] Their Honours agreed and found that the information was not something 'made' or 'artificially created'.

In the circumstances, because claims to nucleotide sequences did not fit within established boundaries, 'wider considerations than Myriad's characterisation of them as an "artificially created state of affairs of

55 Ibid 516 [204]–[205].

56 Ibid 516–17 [210].

57 *D'Arcy* (2015) 258 CLR 334, 351 [28].

58 Ibid 372 [91].

59 Ibid 371–2 [90].

economic utility" come into play'.[60] The plurality then propounded four additional factors that apply when a new class of claim involves a significant new application or extension of the concept. In summary, these are:

> *3. whether patentability would be consistent with the purposes of the Act and, in particular:*
>
> *3.1 whether the invention as claimed, if patentable under s 18(1)(a) could give rise to a large new field of monopoly protection with potentially negative effects on innovation;*
>
> *3.2 whether the invention as claimed if patentable under s 18(1)(a) could, because of the content of the claims, have a chilling effect on activities beyond those formally the subject of the exclusive rights granted to the patentee;*
>
> *3.3 whether to accord patentability to the invention as claimed would involve the court in assessing important and conflicting public and private interests and purposes;*
>
> *4. whether to accord patentability to the invention as claimed would enhance or detract from the coherence of the law relating to inherent patentability;*
>
> *5. relevance to Australia's place in the international community of nations:*
>
> *5.1 Australia's obligations under international law;*
>
> *5.2 the patent laws of other countries; and*
>
> *6. whether to accord patentability to the class of invention as claimed would involve law-making of a kind which should be done by legislature.*[61]

Of these factors, the judges stated that factors 3, 4 and 6 are most important. Particularly persuasive to the judges was the odd consequence that if the claims are properly the subject of a patent, the patent could be infringed without the infringer being aware of that fact. That consequence coupled with the very large size of the relevant class of isolated nucleotide sequences (or nuclei acids as their Honours

[60] Ibid 350 [27].

[61] Ibid.

referred to them), raised the risk of a 'chilling effect upon legitimate innovative activity outside the formal boundaries of the monopoly.'[62]

Gageler and Nettle JJ

Justices Gageler and Nettle focused more on the consideration of inventiveness in their judgment, noting that the process of isolating nucleotide sequences from the cell is a matter of longstanding practice.[63] Their Honours were of the view that, although the isolation of the nucleotide sequence comprising the BRCA1 gene is a man-made process, it does not involve any element of inventiveness. It is no more than the application of a well-known diagnostic technique to a known purpose of examining fragments of human DNA. On this basis, they found that the invention claimed makes no contribution to the manufacture of the substance.[64]

Gordon J

Justice Gordon found that the interrelationship between the isolation of the nucleotide sequence and the identification of the characteristic demonstrates why claim 1 is not a claim to a patentable product.[65] According to her Honour this was the case for a number of reasons, including that: the claim is to multiple products, not a single product; Myriad cannot identify the boundaries of the claim by reference to the chemical composition of the product; Myriad did not create, make or alter the code; there is no idea, concept or principle embodied in a manner of new manufacture; and the claim is too broad.

3.5 IP AUSTRALIA PRACTICE NOTE

Following the High Court's judgment on 16 October 2015, IP Australia issued a draft Examination Practice for public consultation.[66] Following completion of the consultation process, changes to the Manual of

62 Ibid 372 [93].

63 Ibid 393 [157].

64 Ibid 392 [155].

65 Ibid 409 [230].

66 'Commissioner's Proposed Revised Examination Practice for Consultation 16 October 2015 to 6 November 2015' (Practice Note, IP Australia, 16 October 2016) <https://www.ipaustralia.gov.au/sites/g/files/net856/f/20151208_proposed_practice_note_consultation.pdf>.

Practice and Procedure were made on 11 January 2016.[67] The Practice Note affirms that isolated naturally occurring nucleotide sequences are excluded from patentability. As well as these, cDNA and synthetic nucleotide sequences, probes and primers, and isolated interfering/inhibitory nucleotide sequences that merely replicate genetic information of a naturally occurring organism are also excluded.

The Practice Note states that in general the law is to be applied on a case by case basis taking into account the principles and approach taken by the High Court. First, for manner of manufacture, consideration needs to be given to the extent to which the claimed invention in substance falls within established categories of eligible subject matter (to which the principles of *NRDC* are relevant). The Note further clarifies that recombinant or isolated proteins, pharmaceuticals and other chemical substances, methods of treatment, methods of applying herbicides, and applications of computer technology are established categories against which *NRDC* principles can be applied. It is only when there is a new 'class of claim' that the additional factors set down by the plurality in *D'Arcy* need to be considered and, according to the Practice Note, this is a task for the Federal Court.

3.6 AUSTRALIAN PATENT OFFICE DECISIONS CONSIDERING THE NUCLEOTIDE SEQUENCE EXCLUSION

Recent decisions of the Australian Patent Office are starting to provide some indication of the impact of *D'Arcy* on the validity of patent claims. The first such case was *Cargill Incorporated v Dow Agro Sciences LLC*,[68] where the claimed invention was aimed at reducing saturated fatty acids in food to meet plant oil requirements for low saturates or no saturates labels in the US. The specification describes the process of fatty acid synthesis in oil and seeds. The delegate found that the substance of the claim was the genetic information in the nucleotide sequence, in line with *D'Arcy*. However, the delegate distinguished the claim from *D'Arcy* because the inventors had codon-optimised the naturally occurring fungal sequence, which changed the genetic information and

[67] '2.9.2.6 Nucleic Acids and Genetic Information' (Manual of Practice and Procedure, Australian Patent Office, 1 August 2017) <http://manuals.ipaustralia.gov.au/patents/adaptive_patents_manual/index.htm#t=national%2Fpatentable%2F2.9.2.6_Nucleic_acids_and_genetic_information.htm>.

[68] *Cargill Incorporated v Dow Agro Sciences LLC* (2016) 123 IPR 300 ('*Cargill*').

distinguished the optimised sequence from its natural form.[69] Thus, as a matter of legal interpretation, the delegate found that *D'Arcy* did not apply because this subject matter was not near the boundaries of patentability.[70]

Another opportunity to consider the *D'Arcy* holding arose in *Arrowhead Research Corporation,* where the invention related 'to the field of interfering RNA compositions for silencing spleen tyrosine kinase (syk) and for the treatment of Syk-related inflammatory condition'.[71] The delegate found that the inventive contribution resided in the identification of specific target sequences, and that the target sequences themselves were crucial to the invention. However, the delegate concluded that while the arrangement of nucleotides or genetic information conveyed by the interfering RNA ('iRNA') incorporated in the RISC complex was an important element of the claimed invention, the manner in which the invention worked was not solely dependent on the sequence of nucleotides in the iRNA.[72] The delegate considered the inventive contribution of the claimed invention and manner in which the invention worked, and on balance found that the factors supported the proposition that the substance of the invention was a pharmaceutical composition rather than genetic information.

In *Sun Pharmaceuticals v Tasmanian Alkaloids*,[73] the relevant patent claimed the mutagenesis of poppy seeds and screening of progeny plants to produce poppies with a higher output of codeine (over other alkaloids). The Patent Office delegate found no evidence that a mutation producing levels of codeine in line with those claimed in the patent, had or would be naturally occurring. Hence, there was no ground to oppose the patent on the basis that the subject matter was naturally occurring (as it was found to be in *D'Arcy*).[74]

---

69 Ibid 309 [41]. Codon optimisation involves switching rare codons [the set of three nucleotides that code for a particular amino acid] with more common codons that code for the same amino acid, thereby increasing the efficiency of protein expression.

70 Ibid 310 [47].

71 *Arrowhead Research Corporation* [2016] APO 70 (13 October 2016) [5].

72 Ibid [13].

73 *Sun Pharmaceuticals Industries (Australia) Pty Ltd v Tasmanian Alkaloids Pty Ltd* [2018] APO 7 (31 January 2018).

74 Ibid [69]–[71].

In *CSIRO v BASF Plant Science GmbH,* the delegate considered two claims where manner of manufacture was an issue post *D'Arcy*.[75] The claimed process uses molecular biology to take nucleotide sequences for the enzymes responsible for the production of long chain polyunsaturated fatty acids ('LCPUFAS') from lower species, and express them in the seed of the transgenic plant. This is useful to increase fatty acids, particularly in food. The delegate found that the substance of claim 19 and dependent claims was the genetic information embodied in the recombinant nucleic acid molecule which encodes the desaturase and elongase enzymes and includes associated regulatory sequences.[76] The delegate found that the combination of enzyme-encoding nucleotide sequences and associated regulatory sequences specified in claim 19 would not necessarily exist naturally in one nucleic acid molecule in any single organism, concluding that the claimed recombinant nucleic acid molecule had been made by human action.[77] Further, claim 26 was directed towards an isolated nucleotide sequence which encoded a polypeptide that, BASF submitted, had been codon optimised. The delegate found that the sequence had been altered from one that occurs naturally in an alga so that it could be expressed in oil crop plants. [78] On this basis it satisfied the manner of manufacture requirement.

These cases illustrate that, provided that there is a convincing argument to show that what is claimed is genetic information that has been altered from the state in which it naturally occurs, and the alteration is material to the invention, the manner of manufacture requirement will be satisfied in accordance with the *D'Arcy* holding. It should be noted that claims relating to methods of using nucleotide sequences are unaffected by the *D'Arcy* decision, provided that they: (a) do not amount to a claim to the nucleotide sequence itself; or (b) do not otherwise invoke adverse consideration of the factors propounded by the plurality in *D'Arcy.* In respect of point (a), in *Commonwealth Scientific & Industrial Research Organisation v Agriculture Victoria Services Pty Limited,*[79] the delegate found that the claimed method related to a technological problem, in that it pertained to artificial selection and breeding of animals and

[75] *Commonwealth Scientific & Industrial Research Organisation v BASF Plant Science GmbH* (2016) 124 IPR 406; [2016] APO 83 (23 November 2016).

[76] Ibid 415 [55].

[77] Ibid 416 [58].

[78] Ibid 416 [66].

[79] *Commonwealth Scientific & Industrial Research Organisation v Agriculture Victoria Services Pty Limited* (2016) 121 IPR 468; [2016] APO 32 (3 June 2016).

plants.[80] Method claims are considered further later in this occasional paper.

Another Patents Office decision that warrants mention is *Meat & Livestock Australia Limited and Dairy Australia Limited v Cargill, Inc.*[81] In that case, the invention related to methods utilising a high density, single nucleotide polymorphism map of the bovine genome. The high density map provided a resource for defining variation in the bovine genome and provided a means to link nucleotide sequences to gene traits. Claim 13, claiming 'an isolated polynucleotide identified according to the method of claim 8', was the subject of particular scrutiny in this case. Both parties filed further written submissions regarding the relevance of *D'Arcy* to this claim. The delegate found that claim 13 was ambiguous.[82] She commented that if the applicant's intention was to claim the isolated polynucleotides harbouring any of the naturally occurring sequences, this would amount to genetic information which had not been made. If this were the case, the isolated bovine polynucleotides claimed in claim 13 would not satisfy the manner of manufacture requirement. However, the delegate rejected the opposition on all grounds except for the issue of clarity of claim 13, which she stated could be rectified by amendment. The decision of the delegate was appealed to the Federal Court of Australia. The judge in that case, Justice Beach, undertook a broad analysis, not only considering the holding in *D'Arcy* relating to nucleotide sequence claims, but also the plurality factors and the consequences for method claims. Justice Beach's decision is considered in detail later in this occasional paper. Before that, some of the earlier Federal Court musings on *D'Arcy* are considered.

3.7 FEDERAL COURT DECISIONS CONSIDERING THE BROADER ASPECTS OF THE *D'ARCY* DECISION

In recent Federal Court decisions, the Court has shown some reluctance to engage with the factorial approach set out by the High Court in *D'Arcy*. *Commissioner of Patents v RPL Central* was the first appellate decision

[80] Ibid 481 [90].

[81] *Meat & Livestock Australia Limited v Cargill, Inc* [2016] APO 26 (6 May 2016).

[82] Ibid [129].

where patentable subject matter was at issue post-*D'Arcy*.[83] Justices Kenny, Bennett and Nicholas found that the implemented business method claim in suit did not reach the *D'Arcy* threshold requirement of 'a new class of claim involving a significant extension of the concept of manner of manufacture' and thus the *D'Arcy* factors did not need to be considered.[84] In the first instance decision in *Gilead Sciences Pty Ltd v Idenix Pharmaceuticals LLC,* Justice Jagot similarly found that the claims in suit, comprising chemical and pharmaceutical compounds, did not fall into a new class of claim and therefore did not require consideration of the *D'Arcy* factors (which her Honour noted are questions of policy).[85]

Some commentators have asserted that the fact that the judges in these cases have not applied the *D'Arcy* factors illustrates that *D'Arcy* has increased uncertainty in patent law.[86] This uncertainty stems from the concern that the lower courts may adopt an 'extended and strained interpretation of *D'Arcy* in order to avoid invoking and subsequently applying the new factors'.[87] Tanya Obranovich comments further that the *D'Arcy* decision has changed the law as it stood for 56 years and that it has reinterpreted the central principle upon which the determination of patent eligibility has been understood to be based.[88] Her concern is that this has introduced uncertainty across a significantly wider scope of technologies than nucleotide sequences. Some law firms have also commented in their news bulletins that this case may cause more uncertainty for them.[89]

---

83 *Commissioner of Patents v RPL Central Pty Ltd* (2015) 238 FCR 27; [2015] FCAFC 177 (15 December 2015).

84 Ibid 54 [119].

85 *Gilead Sciences Pty Ltd v Idenix Pharmaceuticals LLC* (2016) 117 IPR 252; [2016] FCA 169 (2 March 2016).

86 William Bartlett, '*D'Arcy v Myriad Genetics Inc* [2015] HCA 35: The Plurality's New Factorial Approach to Patentability Rearticulates the Question Asked in *NRDC*' (2016) 24(1) *Journal of Information, Law and Science* 1, 23; Jessica Lai, 'Gene-related Patents in Australia and New Zealand: Taking a Step Back' (2015) 25 *Australian Intellectual Property Journal* 181, 193.

87 Bartlett, above n 86.

88 Tanya Obranovich, 'Biotechnology and Patentability: Navigating Unchartered Waters' on *Managing Intellectual Property* (15 February 2016) <http://web.a.ebscohost.com/ehost/detail/detail?sid=7b15977a-adfa-4550-b603-c7c56243130e%40sessionmgr4009&vid=0&hid=4207&bdata=JnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#AN=112996787&db=buh>.

89 *High Court of Australia Goes Cold on Patentability of Isolated Nucleic Acid* (8 October 2015) Clayton Utz <https://www.claytonutz.com/knowledge/2015/october/high-court-of-australia-goes-cold-on-patentability-of-isolated-nucleic-acid>; Kate Hay and Jacky Mandelbaum, *A Myriad of Considerations: the High Court finds Gene Patent Invalid*

Rebekah Gay and Tom Gumley also express some concern about the impact of the judgment of Gageler and Nettle JJ. As noted earlier in this occasional paper, while their Honours accepted that isolated nucleotide sequences are the products of human action, they rejected their patentability on the basis that they do not meet a threshold level of inventiveness.[90] This inventiveness threshold was articulated in the earlier High Court case of *NV Philips Gloeilampenfabrieken v Mirabella International Pty Ltd* ('*Philips'*) with regard to inventive step.[91] However, the uncertainty that this concept was thought to introduce led to a later High Court decision in *Lockwood v Doric* rejecting any notion that *Philips* introduced a broad threshold test.[92] Concern that the judgment of Gageler and Nettle JJ might lead to the re-introduction of this threshold test may be warranted. Post-*D'Arcy*, this argument was run by the applicant in *Merial New Zealand v Jurox* on the basis that the synergy of anthelmintics was neither new nor inventive.[93] However, this argument could not be sustained on the facts and the delegate held that the claims were to a valid manner of manufacture.

3.8 THE FEDERAL COURT DECISION IN *MEAT AND LIVESTOCK AUSTRALIA V CARGILL*

A further opportunity for the Federal Court to scrutinise the *D'Arcy* decision, including both the breadth of the nucleotide sequence holding and the applicability of the factorial approach, arose in *Meat & Livestock Australia Limited and Dairy Australia Limited v Cargill, Inc.*[94] As noted earlier in this occasional paper, the claims in issue related primarily to methods of using single nucleotide polymorphisms to link nucleotide sequences to gene traits. As such, Beach J was given the opportunity to

(16 October 2015) Corrs Chambers Westgarth <http://www.corrs.com.au/publications/corrs-in-brief/a-myriad-of-considerations-the-high-court-finds-gene-patent-invalid/>; Trevor Davies and Linda Govenlock, *High Court Unanimously Finds Isolated Genetic Material Not Patentable* (8 October 2015) Allens Linklaters <http://allensip.blogspot.com.au/2015/10/high-court-unanimously-finds-isolated.html>.

90 Rebekah Gay and Tom Gumley 'Patents: *D'Arcy v Myriad Genetics*: What Next for Gene Patents in Australia' (2015) 18 *Law Society of NSW Journal* 70, 72.

91 *NV Philips Gloeilampenfabrieken v Mirabella International Pty Ltd* (1995) 183 CLR 655.

92 *Lockwood Security Products Pty Ltd v Doric Products Pty Ltd [No 2]* (2007) 235 CLR 173.

93 *Merial New Zealand Ltd v Jurox Pty Ltd* [2017] APO 5.

94 *Meat & Livestock Australia Limited v Cargill, Inc* (2018) 354 ALR 95; [2018] FCA 51.

consider what extra inventiveness is needed when what is claimed is a method of using excluded subject matter.

In relation to the method claims, Justice Beach distinguished *D'Arcy* primarily on the basis that the claims were not purely to naturally occurring genetic information.[95] His Honour considered the claims to be 'within the plain vanilla concept of manner of manufacture as outlined in *NRDC* and [*D'Arcy*] rather than a new class of claim'.[96] Taking a sample and analysing the sample to identify single nucleotide polymorphisms associated with particular traits of interest was sufficient, in his Honour's view, to give rise to an artificially created state of affairs.[97] Justice Beach then went on to consider how the *D'Arcy* factors might apply, rejecting an assertion that upholding patentability would render the decision inconsistent with *D'Arcy*. His Honour restated his conclusion that the claims in issue were to methods applying information rather than to information per se.[98] Further he found no lack of coherency with foreign law, and rejected an assertion that the 'exorbitant' breadth of the claims would likely have a substantial chilling effect on innovation.[99] On this point, he did find that that the claims were too broad, lacked clarity and were poorly defined, and instructed the parties to amend the patent application.[100]

Justice Beach also considered two product claims, one to an isolated DNA sequence (claim 13) and another to a cloned bovine (claim 11), both resulting from methods claimed in the patent. The sequence claim was rejected, as it fell within the bar created by *D'Arcy.*[101] In contrast, Justice Beach found the claim to the cloned animal to be patentable subject matter, in marked contrast to the decision of the US Federal Circuit in *re Roslin Institute (Edinburgh)*.[102] The basis for his decision was that:

> *the cloned cow in one sense is the same as that which it clones. MLA says superficially that it is 'mere genetic information on a grander scale' and accordingly Myriad is directly applicable. The submission has a superficial allure, but I reject it. An artificial object of economic significance is produced for its own*

95 Ibid 205–7 [425]–[433].

96 Ibid 206 [428].

97 Ibid 211 [455].

98 Ibid 216 [487].

99 Ibid 218 [496]

100 Ibid 178–9 [265]–[266], 219 [500].

101 Ibid 202 [409], 215 [482].

102 *In re Roslin Institute (Edinburgh),* 750 F 3d 1333 (Fed Cir, 2014).

> *sake, not merely as a receptacle for its informational content.*[103]

Justice Beach's comment illustrates the divergence in approaches between the US and Australia. This case is discussed further in Chapter 8.

[103] *Meat & Livestock Australia Limited v Cargill, Inc* (2018) 354 ALR 95; [2018] FCA 51 [470].

CHAPTER 4

THE GENETIC DIAGNOSTIC TESTING INDUSTRY IN AUSTRALIA

4.1 GENETIC DIAGNOSTIC TESTING PROVIDERS

As a first step in analysing the impact of nucleotide sequence and method patent claims on consumer access to and pricing of genetic diagnostic testing, it is necessary to have some understanding of the industry itself. There is some diversity in the types of organisations operating in this space. Traditionally, genetic testing has been performed by public pathology labs, either connected with or independent of public hospitals. Over time, a private industry has emerged. It seems likely that the private sector will expand as the demand for genetic diagnostic testing grows and as new technologies change the ways in which genetic testing services are delivered. For example, next generation sequencing machines, though expensive in themselves, require much less lab infrastructure than traditional testing methods. This means that in the future, once a lab has invested in sequencing machines it is relatively easy in financial terms to start to offer genetic diagnostic testing services. However, there is an increasing regulatory burden on providers, which may deter some market entrants.

It is surprisingly difficult to get a clear picture of the constituents of the genetic diagnostic testing industry and the development of the industry over time in Australia. One reason is that in the past the regulation of the industry was decidedly 'light touch'. The National Association of Testing Authorities ('NATA') was established many years ago, in 1947 and was formally recognised by the federal government as Australia's national provider of lab accreditation service in 1988.[104] However, there was no mandatory requirement for labs offering genetic diagnostic testing services to be accredited by NATA unless they sought reimbursement for tests from the Medicare Benefits Scheme ('MBS').

The role of the MBS in reimbursement for the cost of genetic diagnostic testing is discussed further below, but for now it is necessary to point out that because so few tests are listed on the MBS, providers could in the

[104] National Association of Testing Authorities, Australia, *Our History* (2018) <https://www.nata.com.au/about-nata/our-history>.

past offer a wide range of tests without being NATA accredited. As such, there was no central clearing house to record participants in the industry, what tests they offered, how many tests they performed and how they priced those tests. The Royal College of Pathologists of Australia ('RCPA') has undertaken valuable work in this area. The RCPA undertook two surveys of genetic testing providers in 2006 and 2011. The 2006 survey involved responses from 52 out of 56 labs that were identified as providing medical genetic testing in Australia.[105] The 2011 survey involved responses from 39 of 42 NATA accredited labs that provided medical genetic testing during that year.[106] One key point from the 2011 survey is that it showed a 2.8 fold increase in volumes of tests from 2006. We understand that the RCPA was commissioned to undertake another survey in 2017.

As alluded to above, in parallel with this increase in volume of genetic testing in Australia, more rigorous regulatory requirements have been imposed on the industry. Although general laws of negligence, consumer protection and the like applied to the genetic diagnostic testing industry, there was no comprehensive regulatory framework until 2002. Pursuant to the *Therapeutic Goods Amendment (Medical Devices) Regulation 2002* (Cth) diagnostic testing kits were considered to be in vitro devices ('IVDs'), requiring registration on the Australian Register of Therapeutic Goods. However, the vast majority of genetic tests were still considered to be exempt from the Register. It was not until 2010 that a comprehensive regime was introduced requiring registration of diagnostic genetic tests as IVDs. The requirement for registration applies to both over-the-counter genetic diagnostic test kits and in-house (or lab-based) genetic diagnostics.[107] One of the conditions of registration is that the lab undertaking the testing be NATA accredited. One consequence of this strengthening of the regulatory requirements on genetic diagnostic testing labs is that it is easier to get a clearer picture of the extent of the industry now than in the past through the NATA website, but only insofar as the testing is therapeutic.

---

[105] Royal College of Pathologists, 'Report of the RCPA Genetic Testing Survey 2006' (Report, 31 July 2009) 7.

[106] Royal College of Pathologists, 'Report of the RCPA Genetic Testing Survey 2011' (Report, December 2012) <https://www.rcpa.edu.au/Library/Practising-Pathology/RCPA-Genetic-Testing/Docs/RCPA-Genetic-Testing-Survey-Report.aspx>.

[107] Therapeutic Goods Administration, *Overview of the Regulatory Framework for In-vitro Diagnostic Medical Devices* (6 July 2011) <https://www.tga.gov.au/overview-regulatory-framework-vitro-diagnostic-medical-devices>; See also Dianne Nicol and Meredith Hagger, 'Direct To Consumer Genetic Testing – A Regulatory Nightmare?' (2013) 198 *Medical Journal of Australia* 501.

NATA lists 45 labs in its genetic testing facility webpages. In Table 3, the labs have been separated out by type. We suspect that the webpages may not be fully up to date as we understand that other foreign entities may have entered the Australian market. Nevertheless, this gives us a reasonably accurate picture of the current Australian genetic diagnostic testing industry. We note that that the Human Genetics Society of Australasia has also in the past operated a useful website listing providers of genetic diagnostic testing services, but this website has now been discontinued and a link is provided that directs users to the NATA website. We have made use of this website in our earlier research.

Table 3 clearly shows that the bulk of genetic testing facilities are located in pathology labs connected with public hospitals or independent of them. There is a geographical spread of these facilities across Australia, with the bulk in New South Wales and Victoria. Some, but not all of these labs offer BRCA testing. Some of the major research institutes and universities also offer genetic diagnostic testing. In particular, the Garvan Institute and the Peter MacCallum Institute offer a diverse array of tests. Peter MacCallum has, for many years, offered BRCA testing.

With regard to the private sector, it should be noted that Genomic Diagnostics took over GTG several years ago. As might be expected given this connection, Genomic Diagnostics offers BRCA testing. Previously, another major private provider of genetic testing and other pathology services in Australia was Healthscope. It is our understanding that the pathology component of Healthscope's business was taken over by Australian Clinical Laboratories in mid-2015. It appears that genetic diagnostic testing is only a small component of this company's business, and only in the fields of haematology and oncology.[108] It does not offer BRCA testing. These developments illustrate the fluidity of the private pathology industry.

[108] Australian Clinical Labs, *Haemotology and Oncology* (2017) <https://www.clinicallabs.com.au/doctor/specialists-services/haematology-oncology/>.

Table 3: Data extracted from the NATA webpages on accredited genetic testing facilities, identified according to sector and geographical location

Pathology labs in public hospitals		Standalone public pathology labs and other non-profit providers		Research institutes/ universities		Private companies		IVF related		Foreign	
Lab	**State**	**Lab**	**State**	**Lab**	**State**	**Lab**	**State**	**Lab**	**State**	**Lab**	**Country**
• ACT Pathology • Alfred Pathology Service • Austin Pathology • Prince of Wales Hospital • Royal Brisbane and Women's Hospital • Royal Hobart Hospital • The Sydney Children's Hospital at Westmead • St Vincent's Hospital (and Pathology) (x3)	ACT Vic Vic NT Qld Tas Vic/ NSW NSW	• Monash Pathology • Pathology North (x2) • Pathology Queensland • PathWest Laboratory Medicine WA • SA Pathology (x4) • South Eastern Area Laboratory Services • Sydney South West Pathology Service (x2) • Victorian Clinical Genetic Testing Services Ltd • Victorian Infectious Disease Reference Laboratory	Vic NSW Qld WA SA NSW NSW Vic Vic	• Garvan Institute of Medical Research (+1, spin out Genome.One) • Griffith University • Peter MacCallum Cancer Center • The University of Melbourne	NSW Qld Vic Vic	• Australian Clinical Labs • Cyto Labs Pty Ltd (spin out from Curtin) • The Sonic group: – Douglass Hanly Moir Pathology – Melbourne Pathology Pty Ltd – Sullivan Nicolaides Pathology • Genomic Diagnostics and associated labs: – QML Pathology – Western Diagnostic Pathology • Genomics for Life Pty Ltd	Vic WA NSW Vic Qld Vic Qld WA Qld	• Concept Fertility Centre • Genea Ltd • Vitus Health Specialist Diagnostics	WA NSW Qld	• Hong Kong Sanatorium and Hospital • Queen Elizabeth Hospital • University Pathology Services • Viafet	Hong Kong Hong Kong Hong Kong Global (NSW)

Another vital component of the genetic diagnostic testing industry is the clinical genetic testing service. This service provides genetic counselling to individuals and their families, and often is the main point of entry into the public system. Most states and territories have a single service, although New South Wales and Victoria have multiple separate services. The service is staffed by clinical geneticists, who are medical specialists, and genetic counsellors, who are allied health professionals. General practitioners and specialists are responsible for referral of their patients for diagnostic testing. The 2011 RCPA Report indicates that 54 per cent of labs reported operating under a formal or informal memorandum of understanding with a local clinical genetics service.[109]

Direct to consumer genetic diagnostic testing is not permitted in Australia, although there are a number of Australian and foreign companies that offer a variety of direct to consumer genetic services. These include ancestry, paternity, diet and health-related (non-therapeutic) tests. The question of how to regulate this sector of the industry is both topical and controversial, and is another area of research interest for us.[110]

4.2 TYPES OF GENETIC DIAGNOSTIC TESTS AND VOLUME OF TESTING

There is considerable overlap between labs in the types of tests they offer, although a number have expertise in specific conditions. Many of the hospitals and research institutes, for example, test for rare conditions. Some labs perform very specific tests (eg monogenetic disease, or heritable cancers). Others are more general and perform a broad range of tests, particularly within the public system. Many labs perform tests in-house using kits they have developed. In many other instances, commercial test kits are used, and in other cases testing is outsourced to labs within Australia or internationally.

Decisions as to which tests particular providers perform are determined to some degree by their level of expertise, and which tests have historically been performed. It is probably fair to say that public providers perform the broadest range of tests, and testing for some conditions is

[109] Royal College of Pathologists, 'Report of the RCPA Genetic Testing Survey 2011', above n 106, 4.

[110] See, for example, Nicol and Hagger, above n 107; Dianne Nicol et al, 'Precision Medicine: Drowning in a Regulatory Soup?' (2016) 3 *Journal of Law and the Biosciences* 281.

only available through clinical genetics services (this is especially the case with some familial cancers). Notwithstanding, the private labs perform a very large volume of tests. Although data on the number of tests performed per lab on an annual basis is not publicly available, the larger groups (eg Sonic Group, Primary Healthcare, the NSW Department of Health and the Victorian Department of Health) perform a sizeable proportion of tests. To give some indication of testing volume, the NSW Department of Health conducts in the vicinity of 80,000 – 100,000 tests per year.

Recently, the volume of patients presenting for testing has increased dramatically. Interviewees from publicly-funded labs reported a sharp incline in the number of tests being performed from 2013, primarily as a result of the 'Angelina effect'. Angelina Jolie's publicisation of her prophylactic mastectomy and oophorectomy has raised awareness of diagnostic testing for inherited conditions. Interestingly, the Tasmanian Department of Health and Human Services reports a steady incline in consults for genetic diagnostic testing from around 800 requests per year (2011/12) to just under 1,400 per year (2014/15).[111] A vast majority of requests relate to familial cancers, primarily breast cancer. An attempt to put a number on how many of the increased presenting cases had valid genetic predispositions illustrated that just seven per cent did not. In other words, publicisation of the availability of genetic diagnostic testing had unearthed many patients with genetic predispositions to develop familial cancers. One interviewee from a standalone public lab in Victoria stated that the rate of patients presenting for testing with no valid basis on which to suspect a BRCA mutation is also likely to be around seven per cent.

Changes in testing technologies are also increasing the amount of testing being performed. Testing methods are rapidly evolving. Traditionally, sequencing technologies have involved single gene and multiple gene (gene panel) sequencing methodologies using chemical-based, Sanger sequencing techniques. These testing methods provide a result that indicates whether a specific gene has particular variations, and are useful where looking for a known mutation causative of a disease. The techniques are well-established and well validated. Their limitations in testing for more complex genetic conditions has resulted in a move to next-generation sequencing, including whole exome and whole genome sequencing. While many Australian labs still use single-gene and panel-based tests (with one interviewee referring to them as the 'gold standard'), many interviewees reported they had moved to employing

[111] Tasmanian Clinical Genetics Service, *Annual Report* (2014–15).

exome sequencing. The basis for this move is the vast amount of data these testing technologies produce, which is likely to afford a more holistic interpretation of test results.

This change in technology presents challenges: the capital investment required to maintain abreast with the newest technologies is substantial. The pace at which the technology is moving is rapid. Machines being used today (for example, Illumina's next generation sequencers employed by many of our interviewees), may well be obsolete in five years' time. This cost of the provision of genetic diagnostic testing is a significant one. It presents issues for industry participants across both the public and private sectors. All but one of our clinical interviewees across both public and private labs indicated that their labs had moved to next generation sequencing techniques where appropriate, with the result that their labs employed both traditional and next generation sequencing methods.

4.3 COSTING AND REMUNERATION FOR GENETIC DIAGNOSTIC TESTING

Cost has always been a major factor in debates surrounding the accessibility of genetic diagnostic testing. The funding model for genetic diagnostic testing is surprisingly complex. Generally speaking, a vast majority of funding for healthcare emanates from federal funding, particularly through the MBS, which funds medical services (including services provided by GPs and specialists, diagnostic imaging, pathology and a host of other services), and the Pharmaceutical Benefits Scheme ('PBS').[112] Genetic diagnostic testing is somewhat of an anomaly in this regard, in that few tests are listed on the MBS and the bulk of funding is provided through state government healthcare budgets. Data obtained by the RCPA in 2011 showed that reimbursement for medical genetic testing in Australia was provided by private patients (19.7 per cent), state governments (39.2 per cent) and federal sources (34.1 per cent).[113] In a majority of instances, testing on interstate samples was reimbursed by the referring lab (73.2 per cent).[114]

[112] Australian Bureau of Statistics, *Health Care Delivery and Financing* (24 May 2012) <http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/1301.0~2012~Main%20Features~Health%20care%20delivery%20and%20financing~235>.

[113] Royal College of Pathologists of Australasia, 'Report of the RCPA Genetic Testing Survey 2011', above n 106, 21.

[114] Ibid. Patients were reimbursed in respect of 12 per cent of tests performed, while the testing lab covered the cost in 11.2 per cent of cases.

Most genetic diagnostic testing is performed by public providers, either through referrals from clinical genetic testing services or directly through referrals from specialists. Patients accessing diagnostic genetic testing through this route are not expected to make any payment. From time to time, patients present privately at public clinics without a referral from a clinician, usually on the basis that they do not meet the risk profile that would result in a referral. In these circumstances, they may be expected to cover the cost of their genetic test from their own pocket, although the public lab may choose not to bill the patient. Charges vary, depending on the type of test, with a range from less than fifty dollars up to more than a thousand dollars. Private insurers in Australia do not fund any genetic diagnostic tests. Private labs rely for their business on patients funding their own tests, reimbursement from the MBS for listed tests, or alternatively, on payment by public labs out of their grant funding allocated by the state. Public labs do often make requests for testing to be undertaken by private labs, particularly for rare diseases.

We (Nicol and Nielsen) conducted our first study of patenting and licensing practices in the Australian medical biotechnology industry in 2002–2003.[115] The study included a survey of managers of genetic diagnostic testing labs. Printed surveys were mailed out to the labs offering genetic diagnostic testing listed on the Human Genetic Society of Australia's website in 2002. The survey included questions on the cost of tests, the results of which are broadly summarised in Table 4. This gives a rough indication of the range of fees, which we have separated out into four categories, illustrating the variability in fee structures. A more fine-grained analysis of the fees charged for particular tests in 2002–2003 compared with current fees is presented in Chapter 5 of this occasional paper.

[115] Dianne Nicol and Jane Nielsen, 'Patents and Medical Biotechnology: An Empirical Analysis of Issues Facing the Australian Industry' (Occasional Paper No 6, Centre for Law and Genetics, 2003).

Table 4: Cost of tests: 2002–2003 Study

	Number of respondents	Percentage of respondents	Fee range
Free	4	13	
Free to in-state patients, fee to others	5	16	$200 - $1500
Some covered by MBS, fee for others	6	19	$35 - $1800
Fee based	6	19	$50 - $1950
No answer	10	32	

The 2011 RCPA survey provides some further insight into the funding of genetic diagnostic tests. The survey asked providers how tests performed in their labs during 2011 were funded. Results showed that approximately 40 per cent of assays undertaken in public labs were funded by the state/territory that performed the test, with the remainder being funded federally (34.1 per cent) or by the patient (19.7 per cent).[116] Approximately three-quarters of assays performed on interstate samples were funded by the referring lab.[117] The costs of 11 per cent of assays performed on samples from outside of the state were absorbed by the lab performing the testing,[118] possibly reflecting the fact that these tests were conducted for private patients who often find it difficult to cover the cost of testing.

The 2011 RCPA Report also considered the quantity of samples sent overseas and reported that in comparison with 2006, the proportion had increased.[119] However, the figure remained a small fraction of overall tests performed (2,744 assays requested from overseas labs,[120] 579,742

[116] Royal College of Pathologists, 'Report of the RCPA Genetic Testing Survey 2011', above n 106, 21.

[117] Ibid 4.

[118] Ibid 21.

[119] Ibid 28.

[120] Ibid 26.

assays performed nationally[121]). Samples were generally sent for diagnostic purposes and constituted molecular genetics assays.[122]

Pricing in public labs is generally calculated on a cost-recovery basis. Health care providers manage test pricing on an individual level, within their allocated budget. The cost of testing is driven by a significant number of factors, including:

- the complexity of the genes involved;
- sequencing equipment capital, operational and maintenance costs;
- the cost of testing materials (eg assays, reagents and commercial test kits);
- the cost of interpretation of test results;
- the cost of support services; and
- significantly, the price tolerated by the market – the presence of competitors will be an important factor in cost determination.

While cost recovery is also an important aspect of pricing for private providers, clearly pricing in this case incorporates some profit margin. The discrepancy between the market for public test providers and that for private providers presents private providers with some scope to charge more per test than prices that would be charged in the public system.

Changing technologies was consistently reported to us as being the most significant factor affecting pricing. Both public and private providers have recently decreased test prices, because the pricing of Sanger sequencing methods has declined. As an example, the cost of doing a single gene assay was around $1,800 a decade ago. That price has now decreased to $50-$800 (depending on the complexity of the gene involved). Whole exome sequencing was previously an expensive exercise but a dramatic fall in the price of conducting exome sequencing means that it will now cost around $1,000 to produce a whole exome sequence. The cost of interpretation is an additional and very significant cost, given the amount of data a whole exome sequence generates. But it does demonstrate the huge impact the price of technological advancement is having on pricing fluctuations within this industry. Having said this, one test provider

[121] Ibid 13.

[122] Ibid 26.

stressed the continuing importance of Sanger sequencing methods in certain circumstances:

> *[N]ext generation sequencing can be a sledgehammer to break a nut. Once you know a particular familial mutation, a simple sanger sequencing … saying do they carry this particular variant, is much more cost effective.*

There are further limits to what may be charged: recently the testing environment has become far more competitive, with a number of new US providers entering the market. In the case of these providers, testing is conducted offshore via an Australian clinician. According to two of our interviewees, this may be because overseas providers are more competitive or because clinicians are not aware that anyone in Australia provides that particular test. Providers in other countries are also impacting on the market – one interviewee mentioned the fact that companies in South Korea offer whole exome sequencing for $500-$600. While this was viewed as a positive factor by our interviewees from health departments, clinicians worried that the price competition may make it extremely difficult to maintain the standard of service currently being provided. In a previous section of this occasional paper, we discussed the fact that some state health departments are beginning to abandon the block funding model that has governed funding for the genetic testing sector. A move away from a system of block funding may also have the effect of encouraging price competition between providers, a fact that was noted by one interviewee, a senior health department official from a jurisdiction that had recently changed its funding model to attempt to achieve this outcome.

4.4 STATE GOVERNMENT FUNDING FOR GENETIC DIAGNOSTIC TESTING

Funding for genetic diagnostic testing at the state level has generally been in the form of block grants, though we understand that this situation is now changing, with more stringent requirements in some jurisdictions for labs to provide more detailed accounts of costs and volume of testing. Our interview data makes it clear that funding within state budgets for genetic diagnostic testing services is complex and involves a considerable amount of speculation. The budget allocated by each state health department is distributed between its clinical genetics service and labs – costing models are generally derived from historical and forecast data on test volumes and costs. Clinical genetics services and labs must work within their budgets. Public patients tested within

their home state generally receive free testing (covered by the budget of the lab doing the testing). Where testing is performed on samples from other states, reimbursement is generally sought from the health department/hospital budget of the patient's home state. Tasmania, for example, sends a vast majority of its samples to Victoria for testing, given that there is very limited capacity for genetic testing in Tasmania. This is reflected in the 2011 RCPA Report.[123]

Clinical genetics services do not automatically provide testing for all patients who request it. Prospective patients' risk profiles are analysed for eligibility based on many factors including family history and health background. Samples provided by private patients (eg patients admitted as private patients in public hospitals or patients who do not meet the required risk profile for testing) may also be tested in publicly-funded labs where necessary: our interviewees from private companies indicated that they would send samples to public labs for testing where necessary. Public labs also send samples to private labs. This might occur where a public lab is too busy to conduct testing in a timely manner, or where a very quick turnaround time is required. One of our interviewees informed us that their state-based BRCA testing lab sometimes sent samples to GTG to be tested on these bases. In some cases, a publicly-funded lab may be the only lab that tests for the particular condition. Generally, reimbursement is sought for tests performed for private patients, although we were made aware that there are often instances where this does not occur due to a perception that the patient would have difficulty covering the cost of the test. In these instances, the testing costs are absorbed by the state health care budget.

One interviewee from a state health department explained the concept of block funding, a model which has prevailed in the area of genetic diagnostic testing. Block funding involves the provision of funding for a particular genetic test to one state-funded provider. This gives labs a virtual monopoly on testing in respect of specific genetic conditions. The Victorian health department has recently moved away from a system of block funding in order to encourage multiple labs to undertake testing for particular genetic conditions and to generate competition. One question that might arise here, however, is whether a reduction in economies of scale and expertise might mean a commensurate rise in the cost of providing testing. One matter that factors strongly into putting a price on testing is being able to optimise the use of equipment and personnel through high volume testing. Not surprisingly, some labs that

[123] Royal College of Pathologists, 'Report of the RCPA Genetic Testing Survey 2011', above n 106, 13, 23.

have developed expertise in areas involving rare diseases remain the only labs to test for those conditions. Labs are more likely to move into broader testing practices in areas where testing demand is high, given that in some circumstances some further capital outlay might be required. The reality so far, however, is that labs remain likely to test in areas in which they have long-term expertise, so that the testing landscape in Victoria had not changed dramatically to date. For example, all of Victoria's BRCA testing is still done by the Peter MacCallum Cancer Centre.

4.5 MEDICARE BENEFITS SCHEDULE

A low level of federal funding is provided for genetic diagnostic testing through the MBS. A very limited number of genetic tests are listed on the MBS for specific indications, including haemochromatosis, Fragile X syndrome, Factor V Leiden and some other inherited thrombophilias. In addition, various tests for chromosomal analysis are also available on the MBS. These include karyotyping and chromosomal microarrays for investigation of developmental delay.[124]

Interestingly, the number of tests reimbursed per annum through the MBS did not alter significantly between 2006 and 2011.[125] In 2011, labs reported the performance of 163,296 MBS-funded assays (excluding 17,882 HLA-typing assays).[126] The proportion of MBS-funded molecular genetic assays increased marginally from 24 per cent (in 2006) to 26 per cent (in 2011) of total assays performed.[127] This federally funded testing comprised 60 per cent molecular genetic assays, 39 per cent cytogenetic assays and 1 per cent biochemical genetic assays. This is despite the addition of several new tests to the MBS,[128] and despite the number of newly developed molecular diagnostic tests offered rising steeply during that period.[129]

---

124 Australian Government Department of Health, *The November 2016 Medicare Benefits Schedule* (7 November 2016) <http://www.health.gov.au/internet/mbsonline/publishing.nsf/Content/Downloads-201611>.

125 Royal College of Pathologists, 'Report of the RCPA Genetic Testing Survey 2011', above n 106, 22.

126 Ibid 21.

127 Ibid 22.

128 Ibid.

129 See ibid 18.

Although an MBS listing merely shifts funding obligations from the state to the Commonwealth, the availability of an MBS funded test could result in increased demand by patients who do not meet current risk profiles for state-funded testing, but nonetheless desire testing. It would be prudent to maintain a watching brief to ascertain whether future RCPA reports indicate increased uptake of tests due to further additions to the MBS in the form of genetic diagnostic tests. Relevantly, the Medical Services Advisory Committee ('MSAC'), which provides advice to the Australian Government on whether a new medical service should be publicly funded, is currently considering the addition of a number of new items related to genetic testing to the MBS.

Two new items have been added since 1 November 2017, which provide reimbursement for testing for BRCA1 and BRCA2 mutations.[130] The first provides BRCA testing for women who have been diagnosed with breast or ovarian cancer. The second permits family members of women with a positive test result to also undergo testing for the same mutation. The implications of these additions are discussed further in Chapter 6 of this occasional paper. The consensus view among our interviewees is that calculating an accurate amount for reimbursement via the MBS is incredibly difficult, and probably unrealistic given the time lag between MSAC making a determination on listing a particular item, and listing taking place. Technological developments soon render current price estimates obsolete. Our interview data indicates that even private providers rarely charge more than the scheduled fee where performing MBS-rebated tests. This is due to the fact that MBS-listed costs become the price the market will tolerate. Paradoxically, while the rebateable costs for conditions such as Fragile X and haemochromatosis ($86.15 and $31 respectively) are now viewed as being less than the cost of performing these tests, the cost for the current BRCA1 listing is `far more generous than the cost of actually performing the test'. Given that this test impacts on such a low proportion of patients with a BRCA1 mutation, the implications of this appear to be presently limited. A broader listing (as occurred in 2017) may well result in a spike in demand for BRCA testing from patients who have been diagnosed with breast or ovarian cancer, or who have a family history of these conditions. Increased demand would be partially practitioner-driven given that patients are unlikely to personally be aware of the MBS additions. Importantly, however, BRCA testing is now informing treatment to a far greater extent

[130] Letter from Michael Ryan to Phillip Truskett AM, Royal Australasian College of Surgeons, 19 December 2016 <https://www.surgeons.org/media/24932828/new-amended-mbs-listings.pdf>.

than in the past, as noted by one interviewee from a state health department:

> *BRCA testing can now inform treatment. Not just treatment with drugs but surgery. We know that some breast surgeons are sending their patients with a cancer diagnosis (for testing) which is not the model for family cancer centres. … We know that breast cancer surgeons are sending their diagnosed patients to our FCCs for BRCA testing to inform whether or not to do mastectomies versus lumpectomies.*

This interviewee reported a significant increase in demand for BRCA testing on the basis of this factor alone, and stated that this had put more pressure on the state funded genetics services funding the testing.

One interviewee from a private testing lab commented that increasing the number of tests listed on the MBS could impact on the viability of the private testing industry. This is because private labs would be reliant on the typically low MBS rebates (which may not cover costs), whereas international competitors can charge any amount. This would affect their ability to compete with international labs. Another from a pathology lab based at a public hospital stated in the context of MBS rebates:

> *Speaking to someone who was connected to the private sector, they were basically saying their genetic service loses money for them in terms of that. … In the public and in the private sector, genomics has to be cross-subsidised by a lot of other forms of testing.*

In other words, this respondent's view was there is not a lot of money to be made from performing MBS-listed tests. One interviewee from a private lab, however, argued for increased MBS listings in respect of genetic testing, stating that '[t]he smaller (private) pathology providers cannot survive on the diminishing returns that Medicare provides.' Another interviewee from a private lab said that it is cost-effective to perform the simpler MBS-listed tests, although the margins are considerably less on the more complex tests. A general conclusion we were able to draw is that state-based health department employees are far more strongly in favour of increasing the number of MBS listings than representatives of privately funded labs. This is unsurprising given the structure and funding model inherent in the industry. For those in public labs, a change in their funding source would have little overall impact.

CHAPTER 5

WHAT WE KNOW ALREADY ABOUT THE IMPACT OF NUCLEOTIDE SEQUENCE AND METHOD PATENT CLAIMS ON GENETIC DIAGNOSTIC TESTING

5.1 THE CHO AND MERZ STUDIES

Concerns about the potential for nucleotide sequence and other patents to impact negatively on the provision of genetic diagnostic tests were first raised in earnest in the academic literature by Mildred Cho, Jon Merz and their colleagues in the US in the early 2000s, in part in response to the action of Myriad in actively enforcing its BRCA-related patent rights. However, they found that these concerns about access to genetic diagnostic testing went far beyond BRCA. Their work demonstrated that a number of patent and licence holders were actively enforcing their patents against genetic test providers either by requiring licences containing objectionable terms, or by refusing to license.[131] Problematic licence terms related to the cost of testing, the quantity of tests that could be performed, which labs the tests could be performed in, and whether further research to improve the quality and specificity of tests was permitted.

Cho et al reported that a number of test providers ceased to perform a genetic test they had previously offered, while a number of others decided not to develop or perform a test because of patent considerations. In total, they identified 22 patents that were being actively enforced at the time, affecting 12 genetic tests.[132] Those genetic tests related to common genetic disorders, including haemochromatosis, Fragile X syndrome, Duchenne muscular dystrophy and Huntington's disease, and to more complex disorders such as Alzheimer's disease and, of course, hereditary breast cancer.

In 2003 we conducted searches of patent databases for equivalent Australian patents. These searches showed that three of these US

[131] Jon F Merz et al, 'Diagnostic Testing Fails the Test' (2002) 415 *Nature* 577; Mildred K Cho et al, 'Effect of Patents and Licenses on the Provision of Clinical Genetic Testing Services' (2003) 5 *Journal of Molecular Diagnostics* 3.

[132] Cho et al, above n 131, Table 2.

patents had direct equivalents in Australia and four others were the subject of Australian patent applications (Table 5). Closely related Australian patents or patent applications (that is, having the same patent holder and subject matter) existed for most of the others. Only three had no direct or closely-related equivalents in Australia. As such, we predicted that the capacity existed at the time for a number of nucleotide sequence patents to be enforced against providers of genetic diagnostic services in Australia.

We recently conducted further searches of the AusPat database to determine the current status of these patents and applications. As can be seen in the last column of Table 5, all granted Australian patents identified in our earlier study have now ceased or expired, and all applications have lapsed, save one application that appears to have been misidentified in our earlier study. This indicates that the threat of enforcement of these particular patents in Australia has now dissipated, in that they have suffered a 'Darwinian fate' as some of our Belgian colleagues have put it.[133] This is not to say that there are no patents that have the capacity to impinge on the genetic diagnostic testing landscape, just that the particular Australian equivalents to patents identified by Cho, Merz and their colleagues no longer occupy this landscape.

[133] Isabelle Huys, Gert Matthijs and Geertrui Van Overwalle, 'The Fate and Future of Patents on Human Genes and Genetic Diagnostic Methods' (2012) 13 *Nature Reviews Genetics* 441.

Table 5: Patents linked to cessation of tests in the US and equivalent Australian patents, as of March-April 2003 and 19 June 2017

Test[134]	US patent[135]	Patent holder	Equivalent AU patent[136]	Related AU patent	Current AU status[137]
Apolipoprotein E	US5508167, US6027896 and US5716828	Duke University		AU677614 and AU200173661	AU677614 – expired AU200173661 – not found
Hereditary breast/ovarian cancer	US5753441 (BRCA1)	Myriad Genetics, Inc		AU691958, AU686004 and AU691331	AU691958 – expired AU686004 – expired, *D'Arcy* AU691331 – expired
	US6051379 (BRCA2)	Oncormed, Inc (exclusively licensed to Myriad)	AU199893216		Lapsed
Duchenne/Becker muscular dystrophy	US5541074	Children's Medical Center Corp		AU633249 and AU200073786	AU633249 – ceased AU200073786 – lapsed
Hereditary haemochromatosis	US5705343, US5712098 and US5753438	Mercator Genetics, Inc	AU733459		Expired

[134] The listed tests are those referred to as being stopped in some genetic testing labs in the United States study by Mildred Cho and her colleagues, above n 131, Table 2.

[135] The US patents that included claims covering the performance of those tests and holders of those patents were also reported in Cho et al, ibid.

[136] Equivalent Australian patents were traced using the AU Published Patent Searching database at http://apa.hpa.com.au:8080/ipapa/qsearch and the European Commission's espacenet database at http://ec.espacenet.com/espacenet/ between 20 March and 9 April 2003. The six digit numbers signify granted patents; nine digit numbers are applications: As reported in Dianne Nicol, 'The Impact of Patents on the Delivery of Genetic Tests in Australia' (2003) 15(5) *Today's Life Science* 22.

[137] Current status was traced using the AusPat quick search facility on 19 June 2017: <http://pericles.ipaustralia.gov.au/ols/auspat/quickSearch.do>.

Myotonic dystrophy	US5955265 and US5977333	MIT and University of Wales College of Medicine		AU199335059	Lapsed	
Canavan disease	US5679635	Miami Children's Hospital Research Institute	AU199473207		Lapsed	
Spino-cerebellar ataxia (SCA1, SCA2, SCA3, SCA6)	US5834183 and US5741645 (SCA1)	Regents of University of Minnesota	No equivalent			
	US6251589 (SCA2)	SRL, Inc	AU199664698		Lapsed	
	US5840491 (SCA3)	Kakizuka, A	No equivalent			
	US5853995 (SCA6)	Research Development Foundation	AU735756		Ceased	
Adenomatous polyposis of the colon	US5352775	Johns Hopkins University		AU199213669	Lapsed	
Charcot-Marie Tooth type 1A	US5780223	Baylor College of Medicine		AU199222265	Lapsed	
	US5691144	Athena Diagnostics, Inc	No equivalent			
Fragile X syndrome	US6107025	Baylor College of Medicine	AU199221854		Lapsed	
Huntington's disease	US4666828	The General Hospital Corp		AU676001 and AU673575	AU676001 – ceased AU673575 – ceased	
Factor V Leiden	US5874256	Rijks Universiteit	AU690644		Expired	

5.2 THE NICOL-NIELSEN STUDY

The 2002–2003 Nicol-Nielsen study of patenting and licensing practices in the Australian medical biotechnology industry was undertaken at the time when the studies undertaken by Cho and Merz in the US were garnering some public and academic attention in other countries, including Australia.[138] It was also at a time when GTG was starting to assert its patent rights over its intron sequence analysis patents (colloquially known as 'junk DNA' patents),[139] and when the strategic alliance between GTG and Myriad was first being made public. Not surprisingly, there was concern amongst providers of genetic testing services at the time that GTG could prevent them from offering BRCA1 and BRCA2 testing. However, it was probably too early to observe any form of coordinated enforcement action on the part of GTG in respect of the BRCA patents for which it was the exclusive licensee.

The survey of labs offering genetic diagnostic testing services, which was undertaken as part of the Nicol-Nielsen study, asked 61 questions about the lab, its clinical activity, research and patent activity, and collaborations. A total of 52 surveys were dispatched. Eighteen were returned (35 per cent response rate). These detailed surveys were supplemented by short telephone surveys conducted in March and April 2003 asking six questions about the lab, the tests it performs, payment of licence fees and/or royalties, receipt of notifications from patent or licence holders, responses to notifications, and views on patents. The six questions were only asked if respondents indicated that they had not returned the written survey. Hence, we were reasonably confident that the telephone survey respondents did not overlap with the written survey respondents. There were thirteen responses to the telephone survey, yielding a total response rate of 60 per cent.

One of the key questions for respondents was whether they were required to pay licence fees or make royalty payments to any patent holder in respect of any of the tests they performed. They were then asked to specify the nature and number of licences in the following categories: genetic test; reagents; PCR; other methods; and other. They were also asked to specify the method of payment (eg up front licence fee, royalty, both). The results are summarised in Table 6. Eleven respondent labs (35 per cent) reported that payments of licence fees and/or royalties were made, but almost all of these (9 out of 11) were

[138] Nicol and Nielsen, above n 115.

[139] The early history of GTG's actions is traced in Dianne Nicol, 'Balancing Innovation and Access to Healthcare through the Patent System - An Australian Perspective' (2005) 8 *Community Genetics* 228.

royalties paid to Roche Inc for use of PCR technology. Although PCR itself is a method, the patent in issue actually claimed a product, the enzyme, taq polymerase, which was required to perform the PCR method. The other two responses to payment of licence fees and/or royalties related to an unnamed test kit and an unsure response. One of the respondents referring to PCR also mentioned other reagents.

Table 6: Payment of licence fees or royalties

Payment of licence fees or royalties?	Number of respondents (per cent)
Yes	Total: 11 (36)
	PCR/taq: 9 (29)
	Other reagents: 1 (3)
	Test kit: 1 (3)
	Unsure: 1 (3)
No	18 (58)
Don't know/no answer	2 (6)

Respondents were also asked whether they had ever received notification from a patent holder that the testing they were performing was the subject of a patent. They were asked to identify the patent involved and state their response to the notification. Only eight (26 per cent) respondents stated that they had received notifications and all of these related to PCR (see Table 7). One of these respondents also commented that they had received a verbal notification concerning the haemochromatosis (HFE) test, but this had not been pursued formally.

Table 7: Notifications

	Number of respondents (per cent)
Yes	Total: 8 (26)
	PCR/taq: 8 (26)
	HFE: 1 (3)
No	23 (74)

On the basis of these results, we concluded that there was little indication that holders of patents related to disease genes were actively enforcing their patents against Australian genetic testing labs at the time that this survey was conducted. Despite this low patent-enforcement activity, 45 per cent of respondents expressed concern that gene patents may negatively affect access to genetic testing services and 52 per cent expressed concern that they could negatively affect prices.[140] However, we recognised at the time that the looming threat that GTG might enforce its exclusivity in respect of BRCA testing remained.

5.3 EUROPEAN STUDIES

Some years after we completed our survey of Australian genetic diagnostic providers, colleagues in Europe examined the impact of nucleotide sequence patents on genetic diagnostic testing from the European perspective. Naomi Hawkins conducted semi-structured interviews with stakeholders involved in public sector genomic diagnostic testing in England and Wales.[141] She sought to elucidate the impact of nucleotide sequence patents from their perspective. She found that 'despite the potential for gene patents to have significant negative consequences for genetic testing, in fact, human gene patents have little or no impact on practice for those developing genetic tests in the public sector in the United Kingdom.'[142] Similarly, in a survey of European clinical genetics labs, Sibylle Gaisser and colleagues found 'only a handful

[140] See further Nicol and Nielsen, above n 115, Results Chapter 6.

[141] Naomi Hawkins, 'The Impact of Human Gene Patents on Genetic Testing in the United Kingdom' (2011) 13 *Genetics in Medicine* 320.

[142] Ibid 320.

of cases in which there was patent enforcement', with only '4% (3/77) of responding public-sector labs [ever having] been prevented from offering a testing service because of a patent-related issue'.[143] Despite these assurances, however, in each case the authors cautioned that the situation could change if patent holders decided to enforce their claimed rights.

5.4 THE US STUDIES COMMISSIONED BY THE SECRETARY'S ADVISORY COMMITTEE ON GENETICS, HEALTH AND SOCIETY

In 2010, the journal *Genetics in Medicine* published a series of studies of the impact of patents on particular genetic diagnostic tests in the US.[144] These studies were undertaken by researchers at the Centre for Public Genomics at Duke University, who analysed how patenting and licensing affect clinical access to genetic testing in the US. The research was requested by the Secretary's Advisory Committee on Genetics, Health, and Society ('SACGHS') as part of its broader study on nucleotide sequence patents and licensing practices and their impact on patient access to genetic diagnostic tests. These studies illustrated that nucleotide sequence patents could have a range of effects on access to healthcare depending on the strategies taken by each patent holder. Of the eight tests studied, five showed evidence of the patent increasing the price of the tests.

Colianni and colleagues considered the impact of nucleotide sequence patents on access to tests for Tay-Sachs and Canavan disease.[145] They found that the Tay-Sachs nucleotide sequence patent covering the HEXA gene did not stifle research as it was never enforced. The Canavan patent over the ASPA gene, in contrast, was restrictively licensed and enforced by Miami Children's Hospital ('MCH'). Clinical research labs and commercial labs received cease-and-desist letters from MCH in 1998, which could have stopped them from sequencing the ASPA gene, stifling basic research and some clinical research. In 2003, a lawsuit launched by groups that had contributed data to the initial research leading to the patents was settled, and after this MCH licensed more freely and allowed

[143] Sibylle Gaisser et al, 'The Phantom Menace of Gene Patents' (2009) 458 *Nature* 207.

[144] Robert Cook-Deegan and Christopher Heaney, 'Introduction - Gene Patents and Licensing: Case Studies Prepared for the Secretary's Advisory Committee on Genetics, Health, and Society' (2010) 12 *Genetics in Medicine* S1.

[145] Alessandra Colaianni, Subhashini Chandrasekharan and Robert Cook-Deegan, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing and Carrier Screening for Tay-Sachs and Canavan Disease' (2010) 12 *Genetics in Medicine* S5.

an exemption for pure research. MCH charged labs a $12.50 royalty fee per test to each licensee. When comparing the two tests the researchers found that the average price for a test for Canavan disease was higher ($199.58) than for an unlicensed Tay Sachs test ($111.50) and this significant difference could reflect the differing patent enforcement strategies.[146]

Cook-Deegan and colleagues considered the impact of nucleotide sequence patents and licensing practices on access to genetic testing for inherited susceptibility to cancer, focusing on breast and ovarian cancers and colon cancers.[147] In the US, Myriad Genetics used its patent rights over the BRCA genes to ensure that it was the only provider of the BRCA tests. Genetic testing for familial colorectal cancer, however, is available from multiple labs. Colorectal cancer-associated genes are also patented, but they have been nonexclusively licensed. The study found that the main effect of patent enforcement appears to relate to volume rather than price and that any price effect attributable to patents is buried in noise and confounding variables. The researchers found that price was hard to compare between the two tests.

Skeehan and colleagues studied the effect of nucleotide sequence patents on Alzheimers tests.[148] According to the researchers, patents have not impeded research in the field. Athena Diagnostics holds exclusive licenses from Duke University for three 'method' patents covering APOE genetic testing (which is linked to late onset Alzheimer Disease). Athena offers tests for APOE and genes associated with early onset, autosomal dominant, Alzheimer Disease for $475.[149]

Powell, Chandrasekharan and Cook-Deegan also examined tests for Spinocerebellar ataxia ('SCA').[150] In the US, Athena Diagnostics holds either a patent or an exclusive license to a patent in the case of six spinocerebellar ataxia variants and two other hereditary ataxias. Athena has enforced its exclusive rights to spinocerebellar ataxia-related patents

146 Ibid S9.

147 Robert Cook-Deegan et al, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers with Colon Cancers' (2010) 12 *Genetics in Medicine* S15.

148 Katie Skeehan, Christopher Heaney and Robert Cook-Deegan, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Alzheimer's Disease' (2010) 12 *Genetics in Medicine* S71.

149 Ibid S74.

150 Ashton Powell, Subhashini Chandrasekharan and Robert Cook-Deegan, 'Spinocerebellar Ataxia: Patient and Health Professional Perspectives on Whether and How Patents Affect Access to Clinical Genetic Testing' (2010) 12 *Genetics in Medicine* S83.

by sending notification letters to multiple labs. This study sampled views of patients and health professionals on access to SCA tests. Roughly half of patient respondents to the study had decided not to get genetic tests due to price, coverage and reimbursement by insurers and health plans, and fear of genetic discrimination. The Athena price for the five most common SCAs is $2,300 when ordered individually. A university genetics lab can reportedly perform the same five SCA tests for $1,500.[151]

Angrist and colleagues considered the impact of gene patents for Long QT syndrome.[152] Exclusively licensed in 2002, DNA Sciences Inc sent cease-and-desist patent enforcement letters to university and reference labs offering Long QT syndrome genetic testing. After this there was no test on the market for a 1- to 2-year period. From 2005–2008, most Long QT syndrome-related patents were controlled by Clinical Data, Inc and its subsidiary PGx-Health. Bio-Reference Laboratories secured countervailing exclusive patent rights starting in 2006, also from the University of Utah, and broke the PGx-Health monopoly in early 2009. This created a duopoly for genetic testing in the United States and expanded the number of genes for which commercial testing is available from 5 to 12. This provides evidence that, in this case, the patents clearly increased the cost of tests.

Chandrasekharan and colleagues considered gene tests for mutations in the HFE gene, which is the single most common cause for hereditary hemochromatosis.[153] Patents owned by Bio-Rad covered the HFE gene, related proteins, screening methods and testing kits. In 2007 Bio-Rad Limited acquired the key intellectual property and sublicensed it widely. In part because of broad, nonexclusive licensing, there are now multiple providers and testing technologies, and research continues. The licensing involves an upfront payment and a per-test fee of $20.

Chandrasekharan and Fiffer studied gene tests for hearing loss.[154] They found that the price of genetic tests for hearing loss did not correlate with patent status alone. The price differential between different gene tests could not be attributed to patents or licensing because most testing

[151] Ibid S66.

[152] Misha Angrist et al, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Long QT syndrome' (2010) 12 *Genetics in Medicine* S111.

[153] Subhashini Chandrasekharan et al, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Hereditary Hemochromatosis' (2010) 12 *Genetics in Medicine* S155.

[154] Subhashini Chandrasekharan and Melissa Fiffer, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Hearing Loss' (2010) 12 *Genetics in Medicine* S171.

probably did not have sublicenses. They found that one of the tests (MTRNR1) was offered by Athena Diagnostics for $365, higher than the price of the test offered by universities and hospitals ($150–$285, average price $210). Athena's higher price is not necessarily because of patents, however, and other factors may contribute to price difference. Testing for the MTTS1 gene, which is not patented, is offered at prices comparable (average price $238) to MTRNR1 by universities and hospital-based providers. That test is not offered by any commercial testing providers, including Athena Diagnostics. They found there was no consistent evidence of a premium in testing prices attributable to patent status.

Chandrasekharan and colleagues analysed tests for cystic fibrosis associated with mutations of the CFTR gene.[155] The University of Michigan and the Hospital for Sick Children ('HSC') chose to license their patent nonexclusively. The research shows how patenting and licensing decisions by the University of Michigan, and the HSC allow for significant research without unduly hindering patient access or commercial markets. The initial license fee for kit licenses is $25,000, which has not changed in over 15 years. An in-house commercial test is $15,000 (plus licensees have to pay 3.6 per cent royalty).[156]

Based on these studies, the SACGHS concluded that there was a 'near perfect storm' developing 'at the confluence of clinical practice and patent law' and there was evidence that patents had already limited the potential of some genetic tests.[157] The SACGHS found that knowledge of the genetic foundations of disease had increased exponentially and, at the same time, the cost of using genetic testing technologies had decreased. Genetic testing is progressively being used to personalise the delivery of medicines and medical treatments.[158] At the same time, the SACGHS concluded that patenting and enforcement strategies in the US threatened to undermine the potential of genetic technology, and that few mechanisms exist under US patent law to mitigate these impacts (for example a compulsory licensing regime or broad research exemption).[159] They posited that while patent incentives are arguably not essential for

[155] Subhashini Chandrasekharan et al, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Cystic Fibrosis' (2010) 12 *Genetics in Medicine* S194.

[156] Ibid S197.

[157] Secretary's Advisory Committee on Genetics, Health and Society ('SACGHS'), 'Gene Patents and Licensing Practices and their Impact on Patient Access to Genetic Tests' (Report, Department of Health and Human Services USA, April 2010) 89.

[158] Ibid 89.

[159] Ibid 89–90.

the development of genetic diagnostic tests, the existence of patents over aspects of genetic technologies threatens to hinder their delivery.[160]

The SACGHS also heard presentations from experts during the course of its study and gathered further information and perspectives on its draft report through the solicitation of public comments.[161] The Committee concluded that there was evidence of denial of access to tests not covered by insurance, difficulties in obtaining second opinions and one instance where a patent dispute restricted access to tests for an 18-month period.[162] Although the Committee found that patents or exclusive licences could stimulate development of a genetic test, they found no instances where possession of exclusive rights was a necessary prerequisite.[163] Ultimately, the Committee recommended the creation of exemptions from patent infringement for use of genetic tests for patient care purposes and for use of patent-protected nucleotide sequences for research purposes.[164]

Although the US government decided not to include the exemptions recommended by the SACGHS in the *Leahy-Smith America Invents Act 2011*, s 27 of the Act expressly required the Director of the US Patent and Trademarks Office to conduct a study into second opinion testing, with a requirement that this study be completed nine months from the Act's date of enactment. Anecdotally we understand that the study has been completed but the report of the study has not been released by the US government.

5.5 MORE RECENT AUSTRALIAN RESEARCH AND OTHER REPORTS OF PATENT ENFORCEMENT ACTIONS

One of us (Nicol) and John Liddicoat undertook another survey of genetic testing providers in 2013.[165] Before the survey was drafted, interviews were conducted with managers from four leading Australian providers of genetic diagnostic testing services to assist with survey design. Email invitations to participate were sent to 37 of the lab managers listed on the NATA website for whom email contact details could be verified. Of

[160] Ibid 90.

[161] Ibid 10.

[162] Ibid 42.

[163] Ibid 2.

[164] Ibid 94–5.

[165] Nicol and Liddicoat, above n 45.

the 37 invitees, 28 accessed the survey and 24 completed it (a response rate of 65 per cent).

The results of this survey showed that the number of respondents actually paying licence fees and/or royalties has decreased from the 2002–2003 survey, largely because the PCR patents had long expired. In the Nicol-Liddicoat study, of the three respondents who reported paying fees, only one identified the relevant test: ACTN3. This genetic test is not linked to a disease, but related to athletic performance.[166] The applicant at the time was listed as GTG,[167] although the applicant now listed on the granted patent is Specialist Diagnostic Services Pty Ltd. The patent, which only claims the genetic diagnostic method, not the nucleotide sequence, was applied for on 15 September 2003 and sealed on 21 August 2008. Litigation regarding the equivalent US patent was ongoing in the US at the time we undertook our survey,[168] but as far as we are aware this was the first time its enforcement has been recorded in Australia.

Notably, more notifications of patent rights from third parties were reported when compared with the earlier study. Questions concerning these notifications were divided into 'before 2010' and 'since the start of 2010', to give us a picture of the changing landscape over time. Nine respondents (37.5 per cent) indicated they had received notifications before 2010, and three respondents (12.5 per cent) indicated they had received notifications since the start of 2010. A number of respondents who identified which test the notification related to said that it was for BRCA. Of the nine respondents that received notifications before 2010, four said they related to BRCA testing, one identified PCR, one could not recall details of the notification, and one stated 'maternal cell contamination testing for prenatal samples using STR methodology' ('maternal-prenatal testing', also known as non-invasive prenatal testing or NIPT – we return to the patent issues associated with this test later in this occasional paper). [169] Of the three respondents who said they received notifications post-2010, one stated 'BRCA', one could not recall and the other again said maternal-prenatal testing.

---

166 Kathryn N North et al, 'A Common Nonsense Mutation Results in Alpha-Actinin-3 Deficiency in the General Population' (1999) 21 *Nature Genetics* 353, 353.

167 Australian patent no 2003258390; US patent no 7615342.

168 *Genetic Technologies Limited v LabCorp* (D Del, Civ No 12-1736-LPS-CJB, 20 December 2012); Blaine Bettinger, '23andMe and LabCorp Sued for Patent Infringement' on Blaine Bettinger, *The Genetic Genealogist* (26 December 2012) <http://www.thegeneticgenealogist.com/2012/12/26/23andme-and-labcorp-sued-for-patent-infringement/>.

169 Erika Check Hayden, 'Fetal Gene Screening Comes to Market' (2012) 478 *Nature* 440.

Interestingly, the majority of respondents indicated that they were unconcerned or only marginally concerned about the risk that third-party patent rights could affect the provision of genetic tests now or in the future. This marks a significant shift in opinion from 2003. One respondent identified the SCN1A patent as being of concern. The SCN1A gene is related to Dravet syndrome, a severe form of childhood epilepsy.[170] This disease requires early diagnosis because seizures can cause brain damage and children can lose the ability to function independently. About 70 to 80 per cent of children suffering from Dravet syndrome can be diagnosed early using a test for the SCN1A gene. The applicants on the Australian patent for SCN1A are Bionomics Ltd and McGill University,[171] and the patent had been exclusively licensed to GTG.[172] There had previously been recorded instances of GTG charging higher prices for the test for SCN1A, than providers in other jurisdictions.[173] However, no respondents to this survey indicated a licence fee had actually been paid for the test, nor that a notification had been received regarding potential infringement.

There is some further commentary on nucleotide sequence patents[174] affecting the cost of healthcare, published through newspaper articles and in the Senate Reports. In the Senate Community Affairs Reference Committee Gene Patent Report, for example, mention is made of a submission from the RCPA that included reference to the enforcement of the IgH and TCR gene rearrangement tests performed on cancer tissue from patients with lymphoproliferative disorders or acute myeloid leukaemia.[175] The Report states that US based patent holder, InVivoScribe Technologies, approached all Australian labs performing the tests and insisted they switch to the exclusive use of the company's kit and method or obtain a sub-licence to use their own tests. The RCPA noted that the cost of the in-house test for labs was $28 per patient (excluding labour and other costs) while the cost of the provider kit was

[170] Victor A McKusick and Paul J Converse, **182389* (8 October 2016) Online Mendelian Inheritance in Man <http://omim.org/entry/182389>.

[171] See Australian patent no 2007201976.

[172] Commonwealth, *Parliamentary Debates,* House of Representatives, 18 October 2010, 524 (Melissa Parke).

[173] Ibid.

[174] Application number 2009238365 was filed on 20/11/2009 but lapsed. Application 2008316288 was filed on 2/10/2008 but lapsed. Application 2010256347 was filed 6/2/2010 but lapsed. All three applications claimed methods only. Application 2008255569 claimed a partial sequence as well as method claims. It was filed on 30/5/2008 but has lapsed. The applicant in all cases was Monoquant Pty Ltd, a spin-out company from Flinders University, which licensed the technology to InVivoScribe.

[175] Community Affairs References Committee, above n 40, [3.35]-[3.36].

$292 per patient (excluding labour).[176] The RCPA had purportedly received evidence of switching to use the provider test kit, or ceasing testing altogether.[177] We had not been informed of this enforcement action in our previous empirical studies. We understand that IP Australia has undertaken some analysis of these patents.

The SCN1A test for Dravet syndrome, referred to above, was raised in the popular press around the time of the Senate Community Affairs inquiry. It was noted that testing for Dravet syndrome had become 'devastatingly rare due to patent-protection issues'.[178] According to the report, GTG threatened to sue Australian public hospitals if they continued testing babies for SCN1A. Dr Deepak Gill, head of neurology at the Children's Hospital at Westmead said that if they could conduct the test on-site, the clinic would test 50 per cent more infants for the gene.[179] John Christodoulou, director of the Westmead Hospital's Western Sydney Genetics program, stated that his lab could not risk performing another version of the SCN1A test because GTG may bar him from testing or may impose a prohibitive royalty. It appears that, as a result, hospitals had to send blood samples to Scotland for testing, at a cost of $1,800. Although this is similar to the fee charged by GTG, Dr Gill advised they chose it in preference to the GTG test because he had more confidence in it. Australia stopped screening all but those children whose medical profiles were most dramatically suggestive of the condition. However, in a written statement to the Senate Committee Inquiry into Gene Patents, Dr Gill stated that he was 'not aware of *any* evidence that the licensing of one lab to carry out the tests has had a significant negative impact on research in the field of SCN1A testing'.[180]

Another news report at around the same time noted that the Victorian Clinical Genetic Testing Service wrote to the scientists who had identified gene mutations for Long QT syndrome, hoping to gain some collegial

---

176 Ibid. See also The Centre of International Economics, *Final Report: Economic Analysis of the Impact of Isolated Human Gene Patents* (Report, The CIE, May 2013) <https://www.ipaustralia.gov.au/sites/g/files/net856/f/reports_publications/economic_analysis_of_the_impact_of_isolated_human_gene_patents.pdf> 118.

177 Royal College of Pathologists of Australasia, Submission No 49 to Senate Community Affairs Committee, *Inquiry into Gene Patents 2009* (2010), based on a personal communication with H Wordsworth dated 6 March 2009.

178 Harriet A Washington, *Deadly Monopolies: The Shocking Corporate Takeover of Life Itself – And the Consequences for Your Health and Our Medical Future* (Doubleday Publishing Group, 2011).

179 Julie Robotham, 'Sick Babies Denied Treatment in DNA Row', *Sydney Morning Herald* (online), 29 November 2008.

180 Senator Bill Heffernan, Submission No 76 to Senate Community Affairs References Committee, *Inquiry into Gene Patents,* 2009–10, 27.

insight when they struck some difficulties in their research.[181] Instead, they received a letter from lawyers informing them that their team was infringing patent rights: an American biotechnology company, PGx-Health, held the Long QT patent. The report states that a licence was eventually negotiated for a large, undisclosed sum and the research continued.[182]

In Canada, following enforcement threats by the US-based company Transgenomics relating to its patents over Long QT Syndrome, lawyers for the Children's Hospital of Eastern Ontario ('CHEO') challenged the validity of the Canadian patent. In a settlement agreement in March 2016, Transgenomic agreed to provide CHEO and all other Canadian public sector labs and hospitals the right to test Canadians for the condition on a not-for-profit basis.[183] Dr Gail Graham, chief and clinical geneticist at CHEO, stated that being able to test for the disorder in Canada will cost half of what it did to send material to a US lab.[184] A recent empirical study concluded that agreements such as those entered into by CHEO, have the potential to positively alter the landscape for genetic testing in Canada by providing a blueprint for achieving access to any patented test on favourable terms.[185]

5.6 THE NUCLEOTIDE SEQUENCE PATENT LANDSCAPE

One of the ongoing challenges in this area has been understanding the extent to which the landscape for genetic diagnostic testing is actually occupied by nucleotide sequence and method patents. The Cho and Merz studies in the early 2000s identifying problematic patents relating to the provision of genetic diagnostic tests in the US, and our mapping of

181 Jane Lyons, 'The Profit Strand', *Sydney Morning Herald* (online), 12 April 2010 <http://www.smh.com.au/national/the-profit-strand-20100411-s0u4.html>.

182 Ibid.

183 Julius Melnitzer, 'Canadian Patent Settlement Sets Model for Not-for-Profit Gene Testing', *Financial Post* (online), 12 April 2016 <http://business.financialpost.com/legal-post/canadian-patent-settlement-sets-model-for-not-for-profit-gene-testing/wcm/3f0ea957-0482-429f-ad8d-586ddc8290f2>.

184 Waubgeshig Rice, 'CHEO Reaches "Historic Settlement" with Gene Patent Owner', *CBC News* (online), 9 March 2016 <http://www.cbc.ca/news/canada/ottawa/cheo-gene-patent-lawsuit-settlement-1.3483433>.

185 Sarah E Ali-Khan and Richard E Gold, 'Gene Patents Still Alive and Kicking: Their Impact on Provision of Genetic Testing for Long QT Syndrome in the Canadian Public Health-Care System' (2017) 19(11) *Genetics in Medicine* 1253.

Australian equivalents described earlier in this occasional paper, provides some assistance in this regard.

In later work in 2005, Kyle Jensen and Fiona Murray used bioinformatics techniques to compare gene sequences that were included in US patents with publicly available human genome sequence information, concluding that 'nearly 20% of human genes are explicitly claimed as US IP'.[186] However, Chris Holman subsequently argued that this overestimated the percentage of human genes subject to patent claims, because not all of the sequences identified in the patents were explicitly claimed.[187] Patent landscaping in other jurisdictions suggests fewer DNA and method patents exist outside the US.[188] Analysis of patterns in filing activity indicate a surge in filing in the 1990s which did not continue into the 20th century. It also revealed that many of the patents filed during the 1990s were not pursued to examination, and others that were granted were allowed to lapse.[189]

To provide a more accurate picture of the impact of individual patent claims on genetic diagnostic testing, a group in Belgium led by Geertrui Van Overwalle undertook a manual claim-by-claim analysis of patents claiming rights linked to the 22 most commonly undertaken genetic diagnostic tests ('the Belgian study').[190] They found that 15 of those tests could potentially be blocked by patents in the US or Europe, in the sense that they would be almost impossible to circumvent if best practice guidelines were followed in performing the required test. A total of 35 patents were identified as having claims that were potentially blocking, 24 in the US and 11 in Europe. Method claims were generally found to be more problematic than sequence claims in terms of being almost impossible to circumvent.

---

186 Kyle Jensen and Fiona Murray, 'Intellectual Property Landscape of the Human Genome' (2005) 310 *Science* 239.

187 Christopher M Holman, 'The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation' (2007) 76 *University of Missouri at Kansas City Law Review* 295.

188 Gregory D Graff et al, 'Not Quite a Myriad of Gene Patents' (2013) 31 *Nature Biotechnology* 404.

189 Ibid; Osmat A Jefferson et al, 'Gene Patent Practice across Plant and Human Genomes' (2013) 31 *Nature Biotechnology* 1086; Michael M Hopkins et al, 'DNA Patenting: the End of an Era?' (2007) 25 *Nature Biotechnology* 185; Jannigie G Kers et al, 'Trends in Genetic Patent Applications: the Commercialization of Academic Intellectual Property' (2014) *European Journal of Human Genetics* 1155.

190 Isabelle Huys et al, 'Legal Uncertainty in the Area of Genetic Diagnostic Testing' (2009) 27 *Nature Biotechnology* 903.

Liddicoat, Nicol and Whitton conducted a follow up study in other jurisdictions, using European Patent Office ('EPO') lists of 'simple' and 'extended' families of the patents identified as blocking in the Belgian study.[191] To be clear, we did not engage in claims analysis, but focused more on the status of the patent families. The results of this study provided evidence that the likelihood the specific set of patents identified by Huys et al could impede genetic testing on a global scale is remote, because many of them were not in force in countries other than the US at the time the study was undertaken. In Australia, for example, four of the relevant extended family patents and two of the simple family patents were in force when the study was undertaken. On this basis, we argued that it would be unwise to extrapolate concerns about the overreach of gene patents from the US, to other jurisdictions. Further, the small set of patents remaining in force at the time the study was undertaken have now expired. This is not to say that there are no relevant patents in the genetic diagnostic testing landscape, only that the patents that have been identified as being most likely to have a pernicious effect are no longer features of that landscape.

5.7 ECONOMIC ANALYSIS OF NUCLEOTIDE SEQUENCE PATENTS

Very few economic studies have been undertaken examining the economic consequences of granting nucleotide sequence patents. Notably, in May 2013 the Centre for International Economics ('CIE') prepared an extensive Report for IP Australia which reviewed the economic impacts of isolated human nucleotide sequence patents.[192] The authors completed a literature review, interviews with stakeholders, analysis of the AusPat patent database, and collected what information they could on the economic activity of relevant organisations.[193] Quantitative analysis was used to estimate the direct impacts of isolated human nucleotide sequence patents.

Among other things, the Report provided an estimate of the number of patents ever granted in Australia based on nucleotide sequences.[194] The estimate was that 61 per cent of patents were for partial sequences, 24 per cent were for full-length sequences and 15 per cent were method only. Of the partial sequence patents, 68 per cent had a counterpart in

[191] John Liddicoat, Tess Whitton and Dianne Nicol, 'Are the Gene Patent Storm Clouds Dissipating? A Global Snapshot' (2015) 33 *Nature Biotechnology* 347.

[192] The Centre of International Economics, above n 176.

[193] Ibid 22.

[194] Ibid 68.

nature. Of the full-length sequence patents, 80 per cent had a counterpart in nature. The authors also found that only a small number of patents based on nucleotide sequences were still in force at the time of writing the Report: 30 per cent of all full-length sequences and 37 per cent of all partial sequences.[195] The authors found that the number of partial sequence patents fell dramatically after the Human Genome Project was completed.[196] The Report states that this international scientific project led to increasing difficulty establishing novelty for nucleotide sequence patents. After the completion of this project, method patents made up much more of the patent cohort.[197]

The Report also considered the impact on price of genetic diagnostic tests of patents, but was unable to draw any firm conclusions.[198] The authors suggested that there was some evidence of a price premium on some genetic diagnostic tests resulting from patents, but noted that patents are just one factor attributable to the cost of a genetic test. Other factors include the 'size' of the gene, and whether it forms part of a panel.[199]

[195] Ibid 72.

[196] Ibid 75.

[197] Ibid 76.

[198] Ibid 119.

[199] Ibid 121.

CHAPTER 6

WHAT WE LEARNED ABOUT THE IMPACT OF IP ON GENETIC DIAGNOSTIC TESTING FROM THE INTERVIEWS

6.1 IMPACT OF IP ON AVAILABILITY OF TESTING

The previous section of this occasional paper provides an account of earlier survey data, media reports and other anecdotal evidence showing that test providers received cease and desist letters on several occasions during the early 2000s. These reports aligned with enforcement action being taken in overseas jurisdictions, particularly the US. In this study, we asked our interviewees to confirm whether or not they had been subject to enforcement action by patent holders at any time. Much of what they reported aligns with what we gleaned from our earlier surveys and interviews in 2002–2003, and in 2013.

A number of interviewees reported receiving cease and desist letters from patent holders or licensees in relation to certain tests. Several interviewees affirmed that their labs had received cease and desist letters in respect of BRCA testing. In the case of publicly funded labs, this enforcement action slowed testing only briefly – testing soon resumed once it became clear that legal proceedings were unlikely to be undertaken and the decision was made by relevant state-based health departments to continue to offer the tests. One interviewee from a standalone pathology lab reported a three to six-month delay in testing due to uncertainty over whether enforcement would ensue. As another interviewee explained:

> *It didn't really affect us, we never stopped testing because of the threat of litigation. I remember when the BRCA thing came out, there was a lot of correspondence between public pathology and the Minister for Health to get advice as to how to proceed. From what I remember at the time it was … you know, proceed as currently until … notified, until a change. … I think there was (sic) some decisions made at a federal government level that then rolled down, and we all went … we'll keep doing what we are doing anyway.*

An interviewee from a state based health department corroborated this:

> *So at the time that … Myriad and GTG were sending out letters to everyone … I have a recollection that if we had to pay the additional cost to GTG to do the test, it would be an additional half a million dollars (per year) at the time to the (state) government.*

At the time state government representatives reportedly met and discussed the possibility of application for a compulsory licence should it become necessary. This interviewee stated that federal government support for this approach was given. Although this course of action was not ultimately necessary because GTG abandoned enforcement action, it highlights the collective power of publicly-funded test providers in averting enforcement action.

In the case of private labs, during the period that the BRCA patent was valid, it would appear that no private lab in Australia (aside from GTG) tested for BRCA mutations. One interviewee from a private lab commented that there were no private providers offering the test at the time and this was probably due to a fear of patent enforcement: 'I literally think that everyone in the private space just thought this is too much hassle, we're not going to do it.' Hence, cease and desist letters (which were largely ignored), were received only by public labs. Another interviewee (from a public lab) indicated that the BRCA patents have almost certainly prevented private labs offering BRCA testing, despite public labs working through the enforcement threat by GTG.

It remains the case that Genomic Diagnostics (having acquired the business from GTG) is the only private provider in Australia offering BRCA testing. It is not clear why more private providers have not entered this market. One possible reason is that private providers are concerned that Myriad's diagnostic method patent claims (which remain on foot in Australia), could be enforced against them. Another reason is that the extended period during which GTG was able to exercise a monopoly in BRCA testing helped establish it in an unassailable market position as the sole private provider. In any case, from the public perspective, any deleterious effects that might result from this are ameliorated, as the provision of testing by the public component of the industry has ensured that a relatively competitive environment has been maintained. The fact that the industry is structured in this manner in Australia has a strongly protective effect in that it insulates the industry from any provider being able to charge excessive prices for tests. One interviewee representative of a state health department who has extensive experience in the genetic diagnostic testing industry observed rather acutely that during his time at a standalone public lab:

> *[A]bsolutely, the lab had cease and desist letters. That happened to all, I think, major labs. The laboratory we were running was a fairly major provider in the public sector and there was a lot of confusion around this. GTG weren't pursuing this and then all of a sudden they were … there were negotiations around that, more informal I think, than formal, but at the end of the day it sort of kept going along. …[W]hat sort of happened there, their main referral source was through the public system at that point in time. So it was sort of a little bit how much do you upset this. They were playing a fine balancing game, as well … as trying to maintain company and shareholder interests and things, but also not impact too much on what might be referred through.*

In our view this point about patent holders relying on public labs as a source of referrals is a critical one, in that it provides one compelling explanation for why enforcement threats are followed through only infrequently. It would appear that GTG made a concerted decision not to proceed with enforcement action and to allow public labs to continue testing. This was probably due primarily to the public backlash that would ensue should enforcement proceedings be taken, but also to the fact that a cessation of referrals from public labs would be detrimental to GTG's business.

There have been few other instances of enforcement. Some interviewees reported paying licence fees to Roche in respect of the use of PCR technology, as reported in our 2002–2003 survey, and several also mentioned enforcement action in respect of haemochromatosis testing (although it hadn't specifically impacted on them). Two interviewees recalled receiving cease and desist letters more recently in respect of the SCN1A patent, which we had also received evidence about in our 2013 survey. Further, one of these interviewees (from a pathology lab based at a public hospital) reported that that they had stopped testing for SCN1A for a period of approximately five years upon receiving a cease and desist letter. Aside from this isolated example, very little of this enforcement action would appear to have resulted in the cessation of testing in this space, particularly in public labs. As one interviewee from a public lab put it (in relation to SCN1A patent enforcement): 'Yes, I vaguely remember that one, again, impact level out of 1 to 10, 1.' These results align with earlier media reports of a cessation in testing, demonstrating that although there may have been instances where testing was affected, this impact was not universal.

Another interviewee from a standalone pathology lab described enforcement action during 2011 when they began testing for Long QT

Syndrome. As we noted above, this issue was reported in the media at the time. The test involved an in-house test rather than a test kit. The patent holder (Transgenomic) demanded an up-front fee and a royalty payment for each patient tested (and subsequently billed). Testing continued after a period of discussion but no follow-up demand for payment was ever received. A strategy of 'wait and see' would appear to have reaped rewards for the lab in question: '[T]esting still continued on, labs still continued on doing their testing and waiting and waiting for the letter to arrive and they didn't ever pursue it.'

Two interviewees mentioned the patented test for FLT3 internal tandem duplication testing for patients with acute myeloid leukemia, held by InVivoScribe.[200] Their view was that this patent had limited impact because the only restriction on clinicians related to use of the InVivoScribe test – alternative methods of testing were available and the strict enforcement practices seen in the Canadian system were not replicated in Australia. According to these interviewees, they used alternative tests that, in their view, were better tests anyway.

A similar situation has arisen more recently with regard to NIPT testing, in that Illumina (which holds patents over the Harmony pre-natal test) and Sequenom (with whom Illumina has pooled its patents), have brought legal proceedings against two Australian companies that use Roche's NIPT test (Sonic and Australian Clinical Laboratories). The breadth of Illumina's process patents were commented on by two interviewees, in that they give broad rights over sequencing cell-free fetal DNA, present in maternal blood. While these patents haven't completely eliminated competition in the NIPT market because there is still scope to employ alternative methods of testing, the outcome of the litigation will be a critical element in the development and use of alternative tests. We come back to the NIPT litigation again later in this occasional paper.

As for future developments, there is still a risk that patents generally may have an impact on the delivery of diagnostic genetic tests in the next generation sequencing sphere. As one interviewee noted:

> *I wonder as we are moving forward … how really complex it becomes if we are doing genomes and exomes and there are patents on just about everything. … [I]n a typical genome, we're*

[200] For discussion of corresponding European patents see *German Supreme Court Upholds and Strengthens Invivoscribe FLT3 Patent Position* (29 March 2016) Market Wired <http://www.marketwired.com/press-release/german-supreme-court-upholds-and-strengthens-invivoscribe-flt3-patent-position-2109605.htm>.

> *finding a million variants. For one patient. So some of those are going to turn out to be something you want to follow up. Then you're not going to sit there and search for patents on all of those. Even if you did find one, who are you going to pay and what are you going to do about it?*

The reality is that, to clinicians, patents do not become a problem until they are enforced and, even then, there have been very few instances in Australia where enforcement has proceeded to the point where it has impacted on delivery of tests. As this particular interviewee commented, Australia is a small market in the scheme of genetic diagnostic testing markets. It would be reasonable to conclude that genetic diagnostic testing remains one instance where patent enforcement threats have never had a significant impact:

> *public pressure generally trumps moves to litigate, and the fact that a substantial component of the testing industry in Australia is publicly funded, means that there is a strong incentive for patent holders to permit some degree of market competition.*

6.2 IMPACT OF IP ON COST OF TESTING

A general consensus across interviewees was that the *D'Arcy* decision will have minimal impact on the cost of genetic diagnostic testing in Australia. If *D'Arcy* is to have any impact at all, this effect is unlikely to be discernible and would be extremely difficult (if not impossible) to separate out. Data indicates that the price of genetic diagnostic testing is fluid, in light of the dramatic technological changes that have occurred over the past few years. One reason why we posit that the impact of *D'Arcy* will be minimal is because the impact of nucleotide sequence patents themselves on the cost of testing has been minimal. Certainly, interviewees acknowledged that patents do impact on the price of testing if commercial kits are used and those kits incorporate a royalty component. As one provider from a research institute stated in response to a question about whether test kits that were subject to a patent are inevitably higher: 'Oh they certainly are. If you use kit based tests which, you know, have those sort of patents (sic) included in them, they are very much higher than the laboratory developed tests.' As to whether the *D'Arcy* decision may have prompted a decline in the cost of commercial test kits, this interviewee responded that instead, 'prices have gone up because of the weak Australian dollar'.

On the whole, however, there was a view that royalty payments feed into costing of tests on only a very limited basis, given the range of other

factors that potentially impact on cost. Changing technology was the biggest factor identified by interviewees as having brought prices down:

> *Oh hugely. It's actually put a lot of pressure on us because of the different type of laboratory and skill set that our scientists need. … [W]e do much more for much less but because we are doing so much more we are under quite a lot of pressure.*

Table 8 provides a comparison of test costs in 2003 and 2017. The 2003 data were obtained in surveys conducted as part of the Nicol and Nielsen study. The 2017 data comprise a combination of publicly available information on costs from pathology providers in Australia, and data obtained during interviews. The data on whole genome sequencing combine publicly available information (2006 and 2017 data) and information gleaned during interviews (2017 data).

Table 8: Price comparison between 2003 data and 2017 data

Test type	Price (public lab): 2003	Price (public lab): 2017	Price (private lab): 2017
Haemochromatosis	$31.50 (no charge to public patients)	$31.00	$60.00 (MBS rebate of $31.00, item no. 73315)
Fragile X	$80–$200	$86.15	$101.30 (MBS rebate of $86.15, item no. 73300)
Cystic Fibrosis	$80 (single gene) - $200 (multiple mutations)	$150	$310
BRCA1 and BRCA2	$1,800–$2,500 (no charge to public patients)	$425–$1,000	$500–$700 for BRCA + extra genes (note MBS item no. 73295 germline BRCA testing $1,119.80)
Inherited cancer predisposition panel (esp. breast, ovarian, prostate, pancreas)	Based on cost per gene	$600 (14 genes)	Overseas company Color Genomics charging US$275 (30 genes) for tests ordered online through a medical practitioner
Single gene test	$200–$1,000	$50–$400 (depending on complexity of gene being tested)	$40–$410
Whole exome	Not available	Approx. $1,000	$1,000–$3,000
Whole genome	In 2006: $14 million	$1,500–$4,500 (depending on level of interpretation of results)	$600–$4,500 (depending on level of interpretation of results)

The table reveals a dramatic decline in test costs in a vast majority of instances, this being due largely to technological developments. The most marked cost reduction clearly relates to whole genome sequencing. BRCA testing is also markedly cheaper now, and interviewees reported

that the cost will continue to decrease. The cost of sequencing other single genes has also decreased, although it is difficult to provide one single comparative figure in this context because there is huge variance in the complexity of different genes. In some cases, it would appear that test prices have actually increased recently. For example, the testing prices of public and private labs for cystic fibrosis, as shown in Table 8, is higher in 2017 than in 2003. This is fundamentally due to the fact that testing methods have changed and knowledge of affected genes is far greater. In other cases, test prices appear to have changed only marginally. As one interviewee from a pathology lab in a public hospital put it:

> *Certainly, … they are still expensive tests. We would have charged $1,500 for a fibrillin test in the past. You'd probably still pay $1,500 but you'd get 20 times as much information. … [T]here will probably be real costs coming down as well. At the moment they are probably similar costs but you're just getting a lot more.*

The costs charged by labs for haemochromatosis and Fragile X tests have also remained fairly steady and they generally reflect the scheduled rebate amount. As pointed out earlier, although these rebate amounts were perceived by interviewees to be very low, they probably reflect the cost of performing the test.

The impact of competition within the market should also not be underestimated. Private providers now face competition from overseas competitors in many aspects of genetic testing. This certainly applies to BRCA testing: as Table 8 reveals, companies like Color Genomics are now offering BRCA panel testing for $275, and marketing aggressively to patients and GPs. This marketing approach (while testing overseas) effectively sidesteps the requirement to be NATA accredited, and as an interviewee from a state health department stated:

> *That sort of thing … has probably had more of an impact on the prices than ever, because, and indirectly, that's probably because now they are allowed to operate and offer those tests whereas in the US Myriad had had them shut down. It's not so much the High Court decision in Australia that's affected it, it's the Supreme Court decision … in the US that's allowed the market in the US to open up … and then those companies have (raised) people's awareness of the costs in Australia. That's probably had more of an effect, I think, than the … High Court decision in Australia.*

Further to this, the impact of patents is more likely to be felt in respect of method rather than nucleotide sequence patents, and this has been the case for some considerable time. Lack of choice over sequencing equipment and methods of use are taken as a given by test providers. Coupled with servicing obligations, there is limited choice for test providers as to use of the equipment and associated sequencing assays of industry monoliths such as Illumina. Illumina manufactures state-of-the-art sequencers, which are used by most test providers in Australia. Illumina has a number of patents over its sequencing hardware, and offers maintenance services in conjunction with its machines. There is strong take-up of servicing by Illumina: they are market leaders in sequencing machines and generally their associated service offerings are taken up. A requirement of NATA accreditation is adherence to a strict maintenance schedule.

Most of the comments made about sequencing companies such as Illumina were positive – their sequencers are extremely good as are their associated services (according to most interviewees using this equipment, although one interviewee was very critical). Nonetheless, there is little doubt that their near-monopoly position influences the cost of genetic testing far more than nucleotide sequence patents would appear to have done. Likewise, Illumina's business model is predicated on use of Illumina reagents with their sequencing machines:

> *I'm sure that they are charging up a lot more for the reagents that we use than it costs them to make them, like a lot, lot more. And I would like to offer our tests for less than they cost, but … we're not sort of marking it up by five times whereas I'm pretty sure that they are. But that's them I guess.*

Illumina's ability to charge high costs for its reagents hinges on test providers continuing to use its sequencing equipment and methods. Although it is possible to use competing reagents,[201] its sequencing hardware relies on use of its sequencing cartridges. The price of hardware was reported to be tied to use of Illumina's reagents. However, it is clear that Illumina's technological supremacy is the predominant factor in its control of the sequencing market:

> *All that it means is that someone has to come up with a new way of sequencing and a new chemistry. Whereas, if you say any method to look at this thing you cannot use, that is quite*

[201] Although note that one interviewee from a standalone pathology lab made a comment that contradicts this: *'Once we go with their sequencers we are pretty much committed to their reagent. I'm not aware of any other that will work on their equipment.'*

> *different. But no one yet has come up with a way that is better than Illumina's way of doing it.*

A further interesting fact that can be gleaned from interviews is that Illumina's strategy in developing its sequencers to be compatible with rival reagents is deliberate. Presenting labs with this choice assists in ensuring maximum uptake of its sequencers. One interviewee estimated Illumina's market share of the sequencing market at 80–90 per cent. Another interviewee commented on the potential for Beijing Genomics Institute ('BGI'), a global sequencing centre based in China, to attain a significant share of the sequencing market. BGI has made great inroads in the development of the next generation of sequencing equipment. Like Illumina, BGI has stringently protected its proprietary position.

CHAPTER 7

CONCLUSION

In conclusion, as we hypothesised, the research we have conducted for this project provides limited evidence that the *D'Arcy* decision has had a quantifiable impact on the cost of genetic diagnostic testing in Australia.

Has enforcement by patent holders impacted on the delivery of genetic diagnostic testing?

Our research demonstrates that there have been no long-term interruptions to testing despite moves to enforce patents in particular instances. An important explanation for the fact that these moves have not been followed through is the size of the Australian genetic diagnostic testing market. Particularly for patent holders based overseas, pursuing publicly funded labs is not as worthwhile as it would be in more populous jurisdictions. It is interesting that the only instances of persistent enforcement in Australia (such as the BRCA example) involve Australian patent holders or licensees. However even these more 'determined' attempts to compel enforcement have met with limited success, as testing in public labs has been allowed to continue.

Private labs are unlikely to enjoy the same immunity from enforcement, as demonstrated by the example of BRCA testing. While we cannot be clear that the decision by private providers to refrain from offering BRCA testing was due directly to Myriad/GTG's enforcement action, it would appear to be an indirect impact. While this has a bearing on the ability of these labs to provide particular testing services, it has limited impact on patients who may still access testing from public labs as either public or private patients.

Has D'Arcy *had an impact on the price of genetic diagnostic testing?*

The structure of the largely publicly-funded Australian industry has also influenced the price of testing. Competition between labs generally and public labs in particular, has to some extent siloed these labs from the effects of patent enforcement, especially with regard to the BRCA patents. Public labs continue testing and charge no more than necessary to permit them to recover costs. Clearly if GTG had continued its enforcement line and charged unreasonable royalties this conclusion

may not be possible. But it is reasonable to assume that further attempts to enforce the BRCA patents would have been met with a similar level of resistance from public labs.

There is no doubt that there are areas where patents do impact on the price of genetic diagnostic testing. Patents held by companies manufacturing test kits have almost certainly been factored into the cost of those kits, but this is not something that our interviewees were overly concerned about. It is accepted as a cost of doing business in this space, and generally interviewees felt that in the instances where commercial kits were purchased (as opposed to kits being developed in-house), they were well worth the premium price paid for them. It is also worth noting that there are many instances where commercial kits are available but tests developed in-house are used in preference. Essentially, test providers use commercial kits where they are available, where they are effective, and where the price charged for them is reasonable. Otherwise, they tend to create their own tests.

One reason why there is no general objection to commercial kits is that they usually involve patented methods. Method patents were viewed by interviewees as involving legitimate claims. This is not necessarily the case where claims are very broad, as may be the case with the NIPT patents held by Illumina and Sequenom. Generally speaking, however, patented testing methods are not viewed as being overly far-reaching. It is worth reiterating that the High Court in *D'Arcy* did not consider method claims, therefore we would not expect the decision to impact on the ability of method patent owners or licensees to enforce these patents.

Method claims extend beyond the provision of tests kits. Patents held by Illumina over sequencing methods, for example, provide it with an unassailable market advantage. Nevertheless, its technology and associated methods have set the industry standard, and interviewees were generally very positive about its IP position.

In short, it is possible that *D'Arcy* may have had some impact on the price that patent holders can charge in respect of tests that infringe patents over patented nucleotide sequences. Our interviews provided very little evidence, however, of knowledge of broad patents over cDNA, let alone compliance with those patents. If providers are unaware of the existence of patents, those patents cannot currently be impacting on price.

If D'Arcy *has had an impact, is this impact quantifiable?*

Even if the *D'Arcy* holding has factored to some degree into the price charged for tests (particularly the BRCA test), it is difficult to see how this

effect could be separated out from the other factors impacting on cost. In a good many cases, dramatic technological development and competitive pressures have undoubtedly had a greater effect on prices charged than the relevant patents. It would therefore be extremely challenging to attempt to quantify the impact of *D'Arcy* on prices charged subsequent to the High Court's decision.

CHAPTER 8

FUTURE ISSUES

We have seen from our interviews that many in the field of genetic diagnostics see the *D'Arcy* decision as correcting an anomaly in patent law. For them, nucleotide sequences as they exist in nature are not and never should have been patentable subject matter. Whether the decision has any practical impact for them is, however, a different question. It is questionable whether nucleotide sequence patents were ever of any real value to their holders in Australia, or a threat to users in the context of genetic diagnostic testing. By the time the *D'Arcy* decision was handed down, the early broad nucleotide sequence patents issued in the 1990s had had their day (if indeed there was ever a day to be had), as illustrated by the fact mentioned earlier that the patent in issue in *D'Arcy* had already expired before the decision was released. This is not to say that no other existing patents and no future applications might be affected by the *D'Arcy* holding.

8.1 FURTHER ANALYSIS OF NUCLEOTIDE SEQUENCE PATENTS AND PATENT PROSECUTION

It was not within the ambit of this project to analyse the validity of nucleotide sequence and method patent claims at the present time, post-*D'Arcy*, nor the prosecution of patent applications including these claims post-*D'Arcy,* although this might be warranted at some stage. A number of researchers have been undertaking such analyses of the US patent landscape both pre- and post-*AMP.* For example, even before the *AMP* case was decided, Greg Graff and colleagues estimated that if the Supreme Court invalidated claims to isolated naturally occurring nucleotide sequences, only a small percentage (just over ten per cent) of the total population of nucleotide sequence patents would be invalidated.[202] The reason they gave for this finding was that the tendency to claim isolated sequences was already steadily decreasing with far more claims to non-natural constructs. Moreover, only 41 per cent of those patents likely to be invalidated claimed human nucleotide sequences. Post-*AMP,* Aboy and colleagues examined patent filings and patent prosecutions for subject matter relating to nucleotide

[202] Graff et al, above n 188.

sequences.[203] They observed that such applications continue to be filed, despite the decision of the Supreme Court invalidating Myriad's patents, although there is an expected drop off in claims referring to 'isolated', 'purified' or 'natural' sequences. As noted by Graff and colleagues pre-*AMP,* there is an observable trend towards more claims to non-natural constructs, as well as method claims.

As far as we are aware, no analysis of patent filing and prosecution patterns have been undertaken in Australia post-*D'Arcy.* It may be appropriate for such analyses to be undertaken at this time, or in the near future. We suggest that it might be particularly worthwhile to examine nucleotide sequence and method patent claims and patent prosecution in the context of agricultural biotechnology. Many patents claiming rights to nucleotide sequences have also been issued in this field. Indeed, it is interesting to note that most of the Australian Patent Office decisions to date considering the applicability of the *D'Arcy* holding have concerned non-human nucleotide sequences and method claims. The impact of *D'Arcy* in this context has been largely unexplored and warrants further scrutiny. Agricultural biotechnology is an important area of innovation in Australia, particularly for government research labs and small biotechnology firms. One cause for concern in the study by Aboy and colleagues was that the number of small firms owning nucleotide sequence-related patents dropped dramatically post-*AMP.*[204] If a similar trend emerges in Australia this could have significant implications for biotechnology innovation in this country. This is an area that is of particular research interest to us and in our view warrants investigation, with particular focus on the costs and benefits of nucleotide sequence and method patent claims. Given that the Federal Court's decision in *Meat & Livestock Australia Limited and Dairy Australia Limited v Cargill, Inc*[205] is likely to be appealed to the Full Court, it may be worthwhile to delay any further analysis until this case is finally resolved.

8.2 PARTICULAR ISSUES WITH DIAGNOSTIC METHOD CLAIMS

We have already alluded to the fact that the *D'Arcy* decision says nothing about patent claims to methods of diagnosis and other methods tied to nucleotide sequences. Respondents to our surveys and interviews have consistently reported less concern for method claims than nucleotide

[203] Mateo Aboy et al, 'Myriad's Impact on Gene Patents' (2016) 34 *Nature Biotechnology* 1119.

[204] Ibid 1122.

[205] (2018) 354 ALR 95; [2018] FCA 51.

sequence claims *per se*. From our interviews and other discussions with researchers and diagnosticians, we put this down to a concern that this subject matter is inherently of the nature of a discovery of something that exists in the natural world, not an invention. Methods, it seems, are better recognised as having the characteristics of inventions. Interviewees in the present study also seemed to accept that there was effort and inventiveness involved in developing a new method. Despite this, method claims could in fact have greater impact on the genetic diagnostic sector. For example, the comprehensive claims analysis undertaken by Huys et al found that in many cases diagnostic method claims could have a more profound blocking effect on diagnostic testing than nucleotide sequence product claims.[206]

8.2.1 US Supreme Court case law

In contrast to Australia, there have been a number of decisions of the US Supreme Court relating to method claims that are having a profound impact on the scope of patentable subject matter. These include computer software methods, computer-implemented business methods and diagnostic methods.[207] As noted by Nicol in a recent book chapter,[208] in each case, the Supreme Court was particularly concerned that the patent claims in issue were apt to pre-empt abstract ideas, laws of nature and natural phenomena, long held to be patent ineligible. A summary of the key points from that chapter follows.

Of particular relevance, the Supreme Court in *Mayo Collaborative Services v Prometheus Laboratories, Inc.* ('*Mayo*')[209] held that a method of comparing and analysing rates of drug metabolism in the human body with reference data failed to satisfy the patentable subject matter requirement on the basis that it amounted to patenting a law of nature. To be patent eligible, another inventive concept would have to be added, amounting to something 'significantly more than a patent upon the natural law itself'.[210] The conclusion of the Court was that the relevant claims included no other elements or combination of elements sufficient to ensure that the patent in practice amounted to significantly more than a patent upon the natural law itself. The Myriad patents in issue in the

206 Huys et al, above n 190.

207 *Bilski v Kappos,* 561 US 593 (2010); *Mayo Collaborative Services v Prometheus Laboratories, Inc,* 566 US 66 (2012) ('*Mayo*'); *Alice Corporation Pty Ltd v CLS Bank International,* 134 US 2347 (2014).

208 Dianne Nicol, 'Gene Patents' in Ian Freckleton and Kerry Petersen (eds), *Tensions and Traumas in Health Law* (The Federation Press, 2017) 401.

209 *Mayo,* 566 US 66 (2012).

210 Ibid 1294.

AMP litigation included method claims as well as product claims to the DNA sequences. The Federal Circuit held that the diagnostic method claims were directed towards patent ineligible concepts: abstract mental processes with no transformative steps.[211] This aspect of the Federal Circuit decision was not appealed to the Supreme Court.

Following *Mayo, AMP* and other Supreme Court decisions, the USPTO developed a broad two-step test for assessing if subject matter requirements have been satisfied:

- Step 1: is the claim directed to a process, machine, manufacture or composition of matter?
- Step 2A: is the claim directed to a law of nature, natural phenomenon, or abstract idea?
- Step 2B: does the claim as a whole clearly not seek to tie up the exception?[212]

Thus, in the US, patents claiming methods of using subject matter derived from the natural or abstract world will be invalid unless the methods themselves are truly innovative.

8.2.2 The Australian High Court on method claims

In Australia, there has been some recent judicial activity on the applicability of the *NRDC* test to method claims, but this provides limited assistance in the context of gene-related methods. The decision of the High Court of Australia in *Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd* (*'Apotex'*) in 2013 (prior to *D'Arcy*) related to patents for methods of medical treatment.[213] There has already been a body of case law in Australia and other jurisdictions on the patentability of methods of medical treatment,[214] but prior to this case the High Court had not been given the opportunity to directly rule on this question. Four of the five judges in *Apotex* (with Hayne J in dissent[215]) held that the new use of a

[211] See Justice Lourie's opinion on these issues in the second Federal Circuit decision: *Association for Molecular Pathology v United States Patent and Trademark Office*, 689 F 3d 1303, 1355 (Fed Cir, 2012) (pages 55-62 of the slip opinion).

[212] United States Patent and Trademark Office, '2014 Interim Guidance on Patent Subject Matter Eligibility' (2014) 79(241) *Federal Register* 74619, 74621.

[213] *Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd* (2013) 253 CLR 284*;* [2013] HCA 50 (4 December 2013) (*'Apotex'*).

[214] Discussed in Justine Pila, 'Methods of Medical Treatment within Australian and United Kingdom Patents Law' (2001) 24 *University of New South Wales Journal* 420.

[215] For Hayne J, the key issue is whether the process produces a product that has economic value, not whether the process has economic value because people

known drug in issue in this case fulfilled the manner of manufacture requirement.

In explaining the decision in *Apotex,* the plurality in *D'Arcy* noted that a key factor was whether according patentability would enhance or detract from the coherence of the law relating to inherent patentability.[216] Their Honours concluded that:

> *[h]aving regard to the established patentability of pharmaceutical products, the exclusion of treatments using such products was anomalous and had no stable logical or normative basis. … Their inclusion was consistent with the existing application of the law and served to enhance its coherence.*[217]

However, in *Apotex*, Crennan and Kiefel JJ in their joint judgment and, separately, Gageler J raised some words of caution about the broader question of patentability of other methods of treatment. For them, the question of whether or not 'the activities or procedures of doctors (and other medical staff) when physically treating patients' satisfy the manner of manufacture requirement was left to be decided.[218] As a consequence, method patents that impose restrictions on the physical treatment of patients could be subject to challenge for failure to satisfy the subject matter requirement in the future. This is unlikely to provide much assistance in the case of methods of diagnosis, however, because such methods are performed outside of the body, and hence do not involve physical treatment as such.

8.2.3 Justice Beach in *Meat and Livestock Australia v Cargill*

Quite how subject matter eligibility will be judged in such cases in Australia is yet to be determined, although Justice Beach provided some indication of how the Australian judiciary might approach this issue in *Meat and Livestock Australia v Cargill*.[219] If his Honour's opinion is anything to go by, it is most unlikely that the Australian courts will adopt anything like the *Mayo* test. He opined that '[t]he exposition of the test (particularly the second stage ("apply it") in *Mayo* is too sweeping for me to work out whether I am acting consistently or inconsistently with its

would pay to use it, relying on *NRDC* for this interpretation: see *Apotex* (2013) 253 CLR 284; [2013] HCA 50 (4 December 2013) particularly at [276]–[277].

216 *D'Arcy* (2015) 258 CLR 334, 372 [93].

217 Ibid 351 [28].

218 *Apotex* (2013) 253 CLR 284, 384 [287] per Crennan and Kiefel JJ; see also 390 [312] (Gageler J).

219 *Meat & Livestock Australia Limited v Cargill, Inc* (2018) 354 ALR 95; [2018] FCA 51.

spirit'[220] when determining what it takes to transform an unpatentable law of nature into a patent-eligible application.[221] He found himself unable to undertake a comprehensive assessment of coherence with foreign laws by considering only 'cherry-picked jurisprudence from one jurisdiction' (the US).[222]

Meat and Livestock Australia v Cargill required the Federal Court to consider the patent-eligibility of a series of method claims for identifying bovine traits from nucleic acid samples using single nucleotide polymorphisms ('SNPs').[223] Justice Beach noted that there was some indication in the plurality's judgment in *D'Arcy* that, because they were not addressing method claims, by implication such claims might be more readily viewed as being within the existing boundaries of patentable subject matter.[224] In regard to Cargill's method claims, Justice Beach distinguished *D'Arcy* because the claims in *Meat and Livestock Australia v Cargill* were not entirely directed to naturally occurring genetic information.[225] The case did not just involve looking at a claim to a nucleic acid molecule and considering whether the invention should be characterised as a chemical structure or as genetic information. Nor did the case just deal with claims that involved the discovery of an objectively observed correlation between genotype and phenotype; this was only the starting point for the analysis of the claims.[226] His Honour held that the claims in issue involved the practical application of the genetic information to a particular use. The claims gave rise to an artificially created state of affairs because they involved the taking of a sample and analysing that sample to identify SNPs associated with particular traits of interest.[227] Thus, the claims were 'within the plain vanilla concept of manner of manufacture as outlined in NRDC and Myriad' and were not at the boundaries of patentable subject matter.[228]

8.2.4 The NIPT litigation

Earlier in this occasional paper, we alluded to issues relating to patents connected with non-invasive prenatal testing ('NIPT'). In 1996 researchers based at Oxford University in the UK discovered a new type

[220] Ibid 217 [492].

[221] Ibid.

[222] Ibid.

[223] Ibid 100–1 [1]–[7].

[224] Ibid 202 [409].

[225] Ibid 205 [426].

[226] Ibid 103 [13].

[227] Ibid 211 [455].

[228] Ibid 206 [428].

of DNA in the blood stream of an expecting mother called cell free fetal DNA, or cffDNA.[229] NIPT utilises the presence of this fetal DNA in the maternal circulation. However, it took over ten years for NIPT to become a mainstream form of testing for fetal abnormalities, requiring significant advances in genomic techniques.[230] Commercial development followed quickly, and by late 2011 four companies were offering NIPT in the US alone. Although the patent landscape for NIPT is growing exponentially, the foundational patent arising from the research conducted at Oxford University has been the main source of concern for the developing NIPT industry because most forms of NIPT are believed to fall within its scope. US6258540 and related patents in other jurisdictions was first assigned to Isis Innovation Ltd, the technology transfer arm of Oxford University. Isis Innovation Ltd awarded worldwide exclusive rights to this patent portfolio to Sequenom in 2005 and assigned the patent to Sequenom in 2014.[231]

In June 2016 Sequenom started infringement proceedings in the Australian Federal Court against Sonic Healthcare, Australian Clinical Labs and Ariosa Diagnostics Inc ('Ariosa') in relation to their prenatal assay patent. Sequenom claimed that the use of Harmony NIPT, supplied by Ariosa, by Sonic Healthcare and Australian Clinical Labs infringes its patent. In August 2016 the respondents filed cross-claims for invalidity of Sequenom's patent. Included in the grounds is lack of patentable subject matter.[232]

In the US, the Federal Circuit Court upheld a decision of the District Court of California in favour of Ariosa, finding that cffDNA was a naturally occurring phenomenon and that the claimed method of using this phenomenon was not sufficiently transformative to be patent eligible.[233] The Supreme Court subsequently refused to grant certiorari to hear an

[229] Y M Dennis Lo et al, 'Presence of Fetal DNA in Maternal Plasma and Serum' (1997) 350 *Lancet* 485.

[230] Rossa W K Chiu and Y M Dennis Lo, 'Non-Invasive Prenatal Diagnosis by Fetal Nucleic Acid Analysis in Maternal Plasma: the Coming of Age' (2011) 16 *Seminars in Fetal and Neonatal Medicine* 88.

[231] Nicol is in the process of writing an article on the NIPT patent and industry landscape with colleagues from the UK and the US. Some of the information presented here comes from that study.

[232] DLA Piper, *The Patentability of Diagnostic Methods in Australia: the Australian sequel to Sequenom, Myriad and Mayo* (24 October 2016) Lexology <http://www.lexology.com/library/detail.aspx?g=4230dae4-843e-4925-a015-fe64c8c68804>.

[233] *Ariosa Diagnostics, Inc. v. Sequenom, Inc*, 788 F 3d 1371 (Fed Cir, 2015).

appeal from the Federal Circuit decision.[234] The Australian litigation will give the Federal Court the opportunity to consider for itself how to apply our manner of manufacture test to method claims grounded in naturally occurring phenomena.

These issues relating to the NIPT method claims, and diagnostic and other method claims more broadly, are important from the policy perspective, given the concerns in the US that allowing claims of this nature could pre-empt all other uses of the subject matter underpinning them. However, given Beach J's resounding rejection of *Mayo* in *Meat & Livestock Australia Limited v Cargill,* and given that he is the first instance judge in the NIPT litigation, it is unlikely that we will see any marked move towards adoption of the preemption doctrine in the Australian courts any time soon.

[234] 'Supreme Court Denies Certiorari in Sequenom v. Ariosa' on Donald Zuhn et al, *Patent Docs* (26 June 2016) <http://www.patentdocs.org/2016/06/supreme-court-denies-certiorari-in-sequenom-v-ariosa.html>.

BIBLIOGRAPHY

JOURNAL ARTICLES

Aboy, Mateo, et al, 'Myriad's Impact on Gene Patents' (2016) 34 *Nature Biotechnology* 1119

Ali-Khan, Sarah E and Richard E Gold, 'Gene Patents Still Alive and Kicking: Their Impact on Provision of Genetic Testing for Long QT Syndrome in the Canadian Public Health-Care System' (2017) 19(11) *Genetics in Medicine* 1253

Angrist, Misha, et al, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Long QT syndrome' (2010) 12 *Genetics in Medicine* S111

Bartlett, William, '*D'Arcy v Myriad Genetics Inc* [2015] HCA 35: The Plurality's New Factorial Approach to Patentability Rearticulates the Question Asked in *NRDC*' (2016) 24(1) *Journal of Information, Law and Science* 1

Chandrasekharan, Subhashini and Melissa Fiffer, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Hearing Loss' (2010) 12 *Genetics in Medicine* S171

Chandrasekharan, Subhashini, et al, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Cystic Fibrosis' (2010) 12 *Genetics in Medicine* S194

Chandrasekharan, Subhashini, et al, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Hereditary Hemochromatosis' (2010) 12 *Genetics in Medicine* S155

Check Hayden, Erika, 'Fetal Gene Screening Comes to Market' (2012) 478 *Nature* 440

Chiu, Rossa W K and Y M Dennis Lo, 'Non-Invasive Prenatal Diagnosis by Fetal Nucleic Acid Analysis in Maternal Plasma: the Coming of Age' (2011) 16 *Seminars in Fetal and Neonatal Medicine* 88

Cho, Mildred K, et al, 'Effect of Patents and Licenses on the Provision of Clinical Genetic Testing Services' (2003) 5 *Journal of Molecular Diagnostics* 3

Colaianni, Alessandra, Subhashini Chandrasekharan and Robert Cook-Deegan, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing and Carrier Screening for Tay-Sachs and Canavan Disease' (2010) 12 *Genetics in Medicine* S5

Cook-Deegan, Robert and Christopher Heaney, 'Introduction - Gene Patents and Licensing: Case Studies Prepared for the Secretary's Advisory Committee on Genetics, Health, and Society' (2010) 12 *Genetics in Medicine* S1

Cook-Deegan, Robert, et al, 'Impact Of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers with Colon Cancers' (2010) 12 *Genetics in Medicine* S15

Gaisser, Sibylle, et al, 'The Phantom Menace of Gene Patents' (2009) 458 *Nature* 207

Gambini, Emanuela, 'In the Aftermath of *D'Arcy v. Myriad Genetics Inc*: Patenting Isolated Nucleic Acids in Australia' (2016) 7(2) *European Journal of Risk Regulation* 451

Gay, Rebekah and Tom Gumley 'Patents: *D'Arcy v Myriad Genetics*: What Next for Gene Patents in Australia' (2015) 18 *Law Society of NSW Journal* 70

Gradishar, William, et al, 'Clinical Variant Classification: A Comparison of Public Databases and a Commercial Testing Laboratory' (2017) 22(7) *Oncologist* 797 doi: 10.1634/theoncologist.2016-0431

Graff, Gregory D, et al 'Not Quite a Myriad of Gene Patents' (2013) 31 *Nature Biotechnology* 404

Hawkins, Naomi, 'The Impact of Human Gene Patents on Genetic Testing in the United Kingdom' (2011) 13 *Genetics in Medicine* 320

Holman, Christopher M, 'The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation' (2007) 76 *University of Missouri at Kansas City Law Review* 295

Hopkins, Michael M, et al, 'DNA Patenting: the End of an Era?' (2007) 25 *Nature Biotechnology* 185

Huys, Isabelle, et al, 'Legal Uncertainty in the Area of Genetic Diagnostic Testing' (2009) 27 *Nature Biotechnology* 903

Huys, Isabelle, Gert Matthijs and Geertrui Van Overwalle, 'The Fate and Future of Patents on Human Genes and Genetic Diagnostic Methods' (2012) 13 *Nature Reviews Genetics* 441

Jefferson, Osmat A, et al, 'Gene Patent Practice across Plant and Human Genomes' (2013) 31 *Nature Biotechnology* 1086

Jensen, Kyle and Fiona Murray, 'Intellectual Property Landscape of the Human Genome' (2005) 310 *Science* 239

Kers, Jannigie G, et al, 'Trends in Genetic Patent Applications: the Commercialization of Academic Intellectual Property' (2014) *European Journal of Human Genetics* 1155

Lai, Jessica, 'Gene-related Patents in Australia and New Zealand: Taking a Step Back' (2015) 25 *Australian Intellectual Property Journal* 181

Liddicoat, John, Tess Whitton and Dianne Nicol, 'Are the Gene Patent Storm Clouds Dissipating? A Global Snapshot' (2015) 33 *Nature Biotechnology* 347

Lo, Y M Dennis, et al, 'Presence of Fetal DNA in Maternal Plasma and Serum' (1997) 350 *Lancet* 485

McKusick, Victor A and Paul J Converse, **182389* (8 October 2016) Online Mendelian Inheritance in Man <http://omim.org/entry/182389>

Merz, Jon F, et al, 'Diagnostic Testing Fails the Test' (2002) 415 *Nature* 577

Mullis, Kary, 'The Unusual Origin of the Polymerase Chain Reaction' (April 1990) *Scientific American* 56

Nicol, Dianne, 'Balancing Innovation and Access to Healthcare through the Patent System - An Australian Perspective' (2005) 8 *Community Genetics* 228

Nicol, Dianne, 'Should Human Genes be Patentable Inventions under Australian Patent Law?' (1996) 3 *Journal of Law and Medicine* 231, 237

Nicol, Dianne, 'The Impact of Patents on the Delivery of Genetic Tests in Australia' (2003) 15(5) *Today's Life Science* 22

Nicol, Dianne and John Liddicoat, 'Do Patents Impede the Provision of Genetic Tests in Australia?' (2013) 37(3) *Australian Health Review* 281

Nicol, Dianne and Meredith Hagger, 'Direct To Consumer Genetic Testing – A Regulatory Nightmare?' (2013) 198 *Medical Journal of Australia* 501

Nicol, Dianne, et al, 'Precision Medicine: Drowning in a Regulatory Soup?' (2016) 3 *Journal of Law and the Biosciences* 281

Nielsen, Jane and Dianne Nicol, 'The Legal Vacuum Surrounding Access to Gene-Based Materials and Data' (2016) 24 *Journal of Law and Medicine* 72

North, Kathryn N, et al, 'A Common Nonsense Mutation Results in Alpha-Actinin-3 Deficiency in the General Population' (1999) 21 *Nature Genetics* 353

Pila, Justine, 'Methods of Medical Treatment within Australian and United Kingdom Patents Law' (2001) 24 *University of New South Wales Journal* 420

Powell, Ashton, Subhashini Chandrasekharan and Robert Cook-Deegan, 'Spinocerebellar Ataxia: Patient and Health Professional Perspectives on Whether and How Patents Affect Access to Clinical Genetic Testing' (2010) 12 *Genetics in Medicine* S83

Saiki, Randall K, et al, 'Enzymatic Amplification of Beta-globin Genomic Sequences and Restriction Site Analysis for Diagnosis of Sickle Cell Anemia' (1985) 230 *Science* 1350

Skeehan, Katie, Christopher Heaney and Robert Cook-Deegan, 'Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Alzheimer's Disease' (2010) 12 *Genetics in Medicine* S71

BOOKS AND EDITED CHAPTERS

Mayan, Maria J, *Essentials of Qualitative Inquiry* (Left Coast Press, 2009)

Nicol, Dianne, 'Gene Patents' in Ian Freckleton and Kerry Petersen (eds), *Tensions and Traumas in Health Law* (The Federation Press, 2017) 401

Nicol, Dianne, '*Myriad Genetics* and the Remaining Uncertainty for Biotechnology Inventions' in Charles Lawson and Berris Charnley (eds), *Intellectual Property and Genetically Modified Organisms: A Convergence in Laws* (Ashgate, 2015) 123

Washington, Harriet A, *Deadly Monopolies: The Shocking Corporate Takeover of Life Itself – And the Consequences for Your Health and Our Medical Future* (Doubleday Publishing Group, 2011)

REPORTS, REVIEWS AND GUIDELINES

'2.9.2.6 Nucleic Acids and Genetic Information' (Manual of Practice and Procedure, Australian Patent Office, 1 August 2017) <http://manuals.ipaustralia.gov.au/patents/adaptive_patents_manual/index.htm#t=national%2Fpatentable%2F2.9.2.6_Nucleic_acids_and_genetic_information.htm>

Advisory Council on Intellectual Property, Commonwealth of Australia, '*Patentable Subject Matter: Final Report*' (2010)

Australian Law Reform Commission, *Genes and Ingenuity: Gene Patenting and Human Health*, Report No 99 (2004)

The Centre of International Economics, *Final Report: Economic Analysis of the Impact of Isolated Human Gene Patents* (Report, The CIE, May 2013) <https://www.ipaustralia.gov.au/sites/g/files/net856/f/reports_publications/economic_analysis_of_the_impact_of_isolated_human_gene_patents.pdf>

'Commissioner's Proposed Revised Examination Practice for Consultation 16 October 2015 to 6 November 2015' (Practice Note, IP Australia, 16 October 2016) <https://www.ipaustralia.gov.au/sites/g/files/net856/f/20151208_proposed_practice_note_consultation.pdf>

Community Affairs References Committee, Parliament of Australia, *Gene Patents* (2010)

Genetic Technologies Ltd, 'A Report to Shareholders' (Annual Report, 9 July 2003)

Royal College of Pathologists, 'Report of the RCPA Genetic Testing Survey 2006' (Report, 31 July 2009)

Royal College of Pathologists, 'Report of the RCPA Genetic Testing Survey 2011' (Report, December 2012) <https://www.rcpa.edu.au/Library/Practising-Pathology/RCPA-Genetic-Testing/Docs/RCPA-Genetic-Testing-Survey-Report.aspx>

Secretary's Advisory Committee on Genetics, Health and Society ('SACGHS'), 'Gene Patents and Licensing Practices and their Impact on Patient Access to Genetic Tests' (Report, Department of Health and Human Services USA, April 2010)

Tasmanian Clinical Genetics Service, *Annual Report* (2014–15)

United States Patent and Trademark Office, '2014 Interim Guidance on Patent Subject Matter Eligibility' (2014) 79(241) *Federal Register* 74619

PAPERS (CONFERENCE, DISCUSSION, SUBMISSIONS, WORKING AND OTHERS)

Heffernan, Bill, Submission No 76 to Senate Community Affairs References Committee, *Inquiry into Gene Patents,* 2009–10

Nicol, Dianne and Jane Nielsen, 'Patents and Medical Biotechnology: An Empirical Analysis of Issues Facing the Australian Industry' (Occasional Paper No 6, Centre for Law and Genetics, 2003)

Royal College of Pathologists of Australasia, Submission No 49 to Senate Community Affairs Committee, *Inquiry into Gene Patents 2009* (2010)

Tasmania Statewide Human Research Ethics Committee, *Minimal Risk Application H0016230* (30 November 2016)

COMMUNICATIONS

Letter from Michael Ryan to Phillip Truskett AM, Royal Australasian College of Surgeons, 19 December 2016 <https://www.surgeons.org/media/24932828/new-amended-mbs-listings.pdf>

CASES

Alice Corporation Pty Ltd v CLS Bank International, 134 US 2347 (2014)

Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd (2013) 253 CLR 284

Ariosa Diagnostics, Inc. v. Sequenom, Inc, 788 F 3d 1371 (Fed Cir, 2015)

Arrowhead Research Corporation [2016] APO 70 (13 October 2016)

Association for Molecular Pathology v Myriad Genetics Inc, 133 US 2107 (2013)

Association for Molecular Pathology v United States Patent and Trademark Office, 653 F 3d 1329 (Fed Cir, 2011)

Association for Molecular Pathology v United States Patent and Trademark Office, 689 F 3d 1303 (Fed Cir, 2012)

Bilski v Kappos, 561 US 593 (2010)

Cancer Voices Australia v Myriad Genetics Inc (2013) 99 IPR 567

Cargill Incorporated v Dow Agro Sciences LLC (2016) 123 IPR 300

Commissioner of Patents v RPL Central Pty Ltd (2015) 238 FCR 27

Commonwealth Scientific & Industrial Research Organisation v Agriculture Victoria Services Pty Limited (2016) 121 IPR 468

Commonwealth Scientific & Industrial Research Organisation v BASF Plant Science GmbH (2016) 124 IPR 406

D'Arcy v Myriad Genetics Inc (2015) 258 CLR 334

Genetic Technologies Limited v LabCorp (D Del, Civ No 12-1736-LPS-CJB, 20 December 2012)

Gilead Sciences Pty Ltd v Idenix Pharmaceuticals LLC (2016) 117 IPR 252

In re Roslin Institute (Edinburgh), 750 F 3d 1333 (Fed Cir, 2014)

Kirin-Amgen Inc v Board of Regents of University of Washington (1995) 33 IPR 557

Lockwood Security Products Pty Ltd v Doric Products Pty Ltd [No 2] (2007) 235 CLR 173

Mayo Collaborative Services v Prometheus Laboratories Inc, 566 US 66 (2012)

Meat & Livestock Australia Limited v Cargill, Inc [2016] APO 26 (6 May 2016)

Meat & Livestock Australia Limited v Cargill, Inc (2018) 354 ALR 95

Merial New Zealand Ltd v Jurox Pty Ltd [2017] APO 5

National Research Development Corporation v Commissioner of Patents (1959) 102 CLR 252

NV Philips Gloeilampenfabrieken v Mirabella International Pty Ltd (1995) 183 CLR 655

Sun Pharmaceuticals Industries (Australia) Pty Ltd v Tasmanian Alkaloids Pty Ltd [2018] APO 7 (31 January 2018)

LEGISLATION AND TREATIES

Intellectual Property Laws Amendment (Raising the Bar) Act 2012 (Cth)

Patents Act 1990 (Cth)

PARLIAMENTARY DEBATES, COMMITTEES AND DOCUMENTS

Commonwealth, *Parliamentary Debates,* House of Representatives, 16 October 1990, 2948 (Geoffrey Prosser)

Commonwealth, *Parliamentary Debates,* House of Representatives, 18 October 2010, 524 (Melissa Parke)

Commonwealth, *Parliamentary Debates*, Senate, 17 September 1990, 2478–82 (John Coulter)

Legal and Constitutional Affairs Legislation Committee, Parliament of Australia, *Patent Amendment (Human Genes and Biological Materials) Bill 2010* (2011)

NEWS ARTICLES

Lyons, Jane, 'The Profit Strand', *Sydney Morning Herald* (online), 12 April 2010 <http://www.smh.com.au/national/the-profit-strand-20100411-s0u4.html>

Melnitzer, Julius, 'Canadian Patent Settlement Sets Model for Not-for-Profit Gene Testing', *Financial Post* (online), 12 April 2016 <http://business.financialpost.com/legal-post/canadian-patent-settlement-sets-model-for-not-for-profit-gene-testing/wcm/3f0ea957-0482-429f-ad8d-586ddc8290f2>

Rice, Waubgeshig, 'CHEO Reaches "Historic Settlement" with Gene Patent Owner', *CBC News* (online), 9 March 2016 <http://www.cbc.ca/news/canada/ottawa/cheo-gene-patent-lawsuit-settlement-1.3483433>

Robotham, Julie, 'Sick Babies Denied Treatment in DNA Row', *Sydney Morning Herald* (online), 29 November 2008

BLOGS, PRESS RELEASES, ONLINE PUBLICATIONS AND WEBSITES

AU Published Patent Searching Database <http://apa.hpa.com.au:8080/ipapa/qsearch>

AusPat Version 2.3, IP Australia, <http://pericles.ipaustralia.gov.au/ols/auspat/quickSearch.do>

Australian Bureau of Statistics, *Health Care Delivery and Financing* (24 May 2012) <http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/1301.0~2012~Main%20Features~Health%20care%20delivery%20and%20financing~235>

Australian Clinical Labs, *Haemotology and Oncology* (2017) <https://www.clinicallabs.com.au/doctor/specialists-services/haematology-oncology/>

Australian Government Department of Health, *The November 2016 Medicare Benefits Schedule* (7 November 2016) <http://www.health.gov.au/internet/mbsonline/publishing.nsf/Content/Downloads-201611>

Bettinger, Blaine, '23andMe and LabCorp Sued for Patent Infringement' on Blaine Bettinger, *The Genetic Genealogist* (26 December 2012) <http://www.thegeneticgenealogist.com/2012/12/26/23andme-and-labcorp-sued-for-patent-infringement/>

Davies, Trevor, and Linda Govenlock, *High Court Unanimously Finds Isolated Genetic Material Not Patentable* (8 October 2015) Allens Linklaters <http://allensip.blogspot.com.au/2015/10/high-court-unanimously-finds-isolated.html>

DLA Piper, *The Patentability of Diagnostic Methods in Australia: the Australian sequel to Sequenom, Myriad and Mayo* (24 October 2016)

Lexology <http://www.lexology.com/library/detail.aspx?g=4230dae4-843e-4925-a015-fe64c8c68804>

Espacenet Patent Search (26 April 2017) European Patent Office <http://ec.espacenet.com/espacenet/>

Genetic Technologies Ltd, 'New Position re BRCA Testing' (Press Release, 2 December 2008)

German Supreme Court Upholds and Strengthens Invivoscribe FLT3 Patent Position (29 March 2016) Market Wired <http://www.marketwired.com/press-release/german-supreme-court-upholds-and-strengthens-invivoscribe-flt3-patent-position-2109605.htm>

Hay, Kate, and Jacky Mandelbaum, *A Myriad of Considerations: the High Court finds Gene Patent Invalid* (16 October 2015) Corrs Chambers Westgarth <http://www.corrs.com.au/publications/corrs-in-brief/a-myriad-of-considerations-the-high-court-finds-gene-patent-invalid/>

High Court of Australia Goes Cold on Patentability of Isolated Nucleic Acid (8 October 2015) Clayton Utz <https://www.claytonutz.com/knowledge/2015/october/high-court-of-australia-goes-cold-on-patentability-of-isolated-nucleic-acid>

National Association of Testing Authorities, Australia, *Our History* (2018) <https://www.nata.com.au/about-nata/our-history>

Obranovich, Tanya, 'Biotechnology and Patentability: Navigating Unchartered Waters' on *Managing Intellectual Property* (15 February 2016) <http://web.a.ebscohost.com/ehost/detail/detail?sid=7b15977a-adfa-4550-b603-c7c56243130e%40sessionmgr4009&vid=0&hid=4207&bdata=JnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#AN=112996787&db=buh>

'Supreme Court Denies Certiorari in Sequenom v. Ariosa' on Donald Zuhn et al, *Patent Docs* (26 June 2016) <http://www.patentdocs.org/2016/06/supreme-court-denies-certiorari-in-sequenom-v-ariosa.html>

Therapeutic Goods Administration, *Overview of the Regulatory Framework for In-vitro Diagnostic Medical Devices* (6 July 2011) <https://www.tga.gov.au/overview-regulatory-framework-vitro-diagnostic-medical-devices>

APPENDIX A

INTERVIEW QUESTIONS/THEMES

1. Can you explain a bit about your lab/organisation/department and its background/function?

2. What is your role in the lab/organisation/department?

3. What tests does your lab perform?
    - Why these tests?

4. How many tests does your lab perform? Can you roughly categorise them into test types?

5. How are the tests paid for – who pays and how are they paid?

6. What tests does your lab do in-house and what tests are sent off?
    - How are the costs of tests calculated and charged in each case?

7. How does your approach to performing and costing tests differ where the test is listed on the MBS?

8. Do patents enter (or have patents in the past entered) into decisions about what your lab tests for?

9. Have these decisions changed where patents have expired, or changed due to the *Myriad* decision?
    - Are you aware of any changes in costing practices because patents have expired, or due to the outcome of the *Myriad* decision?

10. How have genetic testing technologies changed over time (eg is your lab changing to exome sequencing or whole genome sequencing)?
    - How does this affect cost?
    - What are the implications of changing technologies in this area?

11. Are there any IP issues that have factored into these decisions?

12. Does your lab perform NIPT?
    - Do you perform this test under licence?
    - What influenced your lab to offer the test/how long have you offered it?
    - What is your understanding of the patent situation in relation to this test?
    - How is this particular test costed and charged?
    - Has there been any change in cost since the test was first offered? What would you attribute this to?